

Approach to the Surgical Management of Resectable Gastric Cancer

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Abstract: The rates of gastric cancer, which is the third leading cause of cancer-related deaths worldwide, vary depending on geographic location. Margin-negative gastrectomy and adequate lymphadenectomy (removal of ≥ 15 lymph nodes) are the cornerstones of multimodal treatment for operable gastric cancer. Diagnostic laparoscopy should be included in the armamentarium for newly diagnosed gastric cancer in order to overcome the limitations of cross-sectional imaging in identifying sub-radiographic hepatic or peritoneal metastases. The benefit of surgical therapy is enhanced by at least 13% when it is integrated with multimodal therapy: either surgery followed by adjuvant chemoradiotherapy or surgery with perioperative systemic therapy. This multidisciplinary approach to treatment will continue to be an evolving paradigm, especially with the emergence of systemic and targeted therapies.

Relevant Epidemiologic Facts

Gastric cancer is the third leading cause of cancer-related deaths worldwide.¹ The incidence is highest in Japan and eastern Asia (approximately 18-25 cases per 100,000 people) and much lower in Europe and North America (approximately 8-10 cases per 100,000 people).² Gastric cancer is currently the 15th most prevalent cancer in the United States, with an estimated 5-year survival rate of 29%. It is estimated that gastric cancer was diagnosed in more than 24,000 Americans in 2015, and that more than 10,000 died of this disease.³

The median age of patients at the diagnosis of gastric cancer is 69 years. Like persons with other solid organ cancers, most of those affected are older adults (>65 years of age).⁴ Recently, the incidence of early gastric cancer has begun to rise in younger adults (<50 years of age). Younger patients are more likely than older adults to present with advanced or metastatic disease at diagnosis. Despite these trends at presentation, younger patients tend to have a more favorable prognosis at each stage compared with their older counterparts.⁵

Race and ethnicity affect the presentation, treatment patterns, and prognosis of gastric cancer. For example, whites are more likely

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to present with proximal disease, whereas Asians typically present with early-stage disease and distal tumors, which carry a more favorable prognosis. In contrast, African Americans and Hispanics are more likely to present with advanced disease and have worse survival outcomes.^{6,7}

Presenting Clinical Features

Patients who have gastric cancer present with a wide array of gastrointestinal symptoms that can easily overlap with those of benign conditions, such as gastroesophageal (GE) reflux and peptic ulcer disease. Most patients present with one or more of the following symptoms: early satiety, dysphagia, epigastric burning/discomfort, and weight loss. Those with advanced disease also may present with more drastic features, such as a palpable abdominal mass, cachexia, bowel obstruction, and ascites.⁸ Metastasis from gastric cancer can be present in the setting of an enlarged supraclavicular lymph node (Virchow's node), enlarged left axillary lymph node (Irish's node), enlarged periumbilical lymph node (Sister Mary Joseph node), or drop metastasis in the pouch of Douglas (Blumer's shelf).⁸ However, it needs to be noted that physical examination alone typically finds metastatic gastric cancer less than 10% of the time; thus, it should not be used as a definitive diagnostic tool.

Diagnostic Considerations at Presentation

History and Physical Examination

A thorough history should be taken and a physical examination performed whenever a patient has suspected (or established) gastric cancer. For the history, the presence of the following should be ascertained: unintentional weight loss, early satiety, GE reflux, anorexia, vomiting, epigastric pain, fatigue, bleeding, tobacco and/or alcohol use, consumption of large amounts of nitrate-preserved and/or smoked foods, and *Helicobacter pylori* infection. Family history is also important; approximately 1% to 3% of gastric cancers can be caused by a germline mutation in the E-cadherin gene (*CDH1*), which leads to a syndrome called hereditary diffuse gastric cancer.⁸

Preoperative Laboratory Workup

To better prepare patients with operable gastric cancer for multimodal therapy, the following parameters need to be obtained and corrected (if needed) before therapy is initiated:

- Complete blood cell count: This is needed to evaluate and treat preoperative gastric cancer-related anemia.
- Basic metabolic panel: This is needed to detect electrolyte imbalances in situations of gastric outlet obstruction. The basic metabolic panel also points toward any renal abnormalities before the patient undergoes contrast-enhanced cross-sectional imaging and subsequent surgical and systemic therapy.

- Liver function panel: It is particularly important to obtain a liver function panel before the induction of preoperative systemic therapy.
- Albumin and pre-albumin levels: Given that 30% to 80% of patients who have newly diagnosed gastric cancer present with underlying malnutrition (albumin <2.5 g/dL), preoperative malnutrition needs to be identified and treated because it is associated with poorer operative outcomes (ie, higher rates of operative mortality, complications, and prolonged hospital stay).⁹

Tumor Markers

The use of conventional tumor markers such as carcinoembryonic antigen (CEA), cancer antigen 19-9 (CA19-9), and CA72-4 to estimate the prognosis, recurrence, and metastasis of advanced gastric cancer has been evaluated. These markers have been related to TMN (tumor, node, metastasis) stage, but their use for the early detection of gastric cancer has been deemed inappropriate owing to their poor specificity and sensitivity.¹⁰ Although they have shown some advantage in estimating prognosis and recurrence, they have not had any effect of increasing survival in patients with diagnosed gastric cancer, especially in the late stages. With these limitations kept in mind, conventional tumor markers can be another helpful tool to detect recurrence after gastrectomy.

Diagnostic and Staging Modalities

Upper Gastrointestinal Endoscopy

To date, upper gastrointestinal endoscopy remains the gold standard to detect and diagnose gastric cancer. Endoscopy allows the operating surgeon to assess the following important therapy-driven factors:

- (1) the proximal and distal extent of the tumor, information that guides the extent of gastric resection;
- (2) whether an R0 (margin-negative) resection is feasible in scenarios of involvement of the distal esophagus or GE junction;
- (3) the presence of linitis plastica, which alerts the multidisciplinary team to potential sub-radiographic micro-metastatic disease;
- (4) the response to preoperative chemotherapy in patients with proximal gastric cancer, in whom preservation of the GE junction leads to a better postoperative functional outcome; and
- (5) tissue profiling in advanced disease (eg, human epidermal growth factor receptor 2 expression status).¹¹

Endoscopic Ultrasound

Endoscopic ultrasound (EUS) is a useful staging tool in gastric cancer. It has the special ability to visualize 5 layers of the gastric wall, which correlate with histologic layers,

for accurate regional staging before therapy. It also informs subsequent staging and treatment strategies. Specifically, it does the following: (1) determines the American Joint Committee on Cancer (AJCC) pre-therapy T and N stages to guide the sequence of therapy (surgery first vs perioperative therapy); (2) enhances information on the extent of disease, especially in patients with proximal gastric cancer; and (3) in combination with esophagogastroduodenoscopy, enhances diagnostic accuracy in detecting linitis plastica.¹²

EUS is operator-dependent and should be performed at high-volume centers, where its accuracy is significantly greater.^{13,14} Although EUS is a useful tool, there are known limitations of its utility that should be noted. EUS is less reliable in accurately distinguishing between a tumor and inflammatory tissue; therefore, it is useful at the initial staging assessment, not the assessment of response after neoadjuvant therapy.¹⁵ Owing to the difficulty of distinguishing between cancer and inflammation, EUS can result in false upstaging in up to 23% of cases.¹⁶ EUS can accurately differentiate T1 and T2 lesions from T3 and T4 lesions, with a sensitivity of 86% and a specificity of 91%, but it is less reliable in detecting nodal disease, in which its sensitivity decreases to 69% and its specificity to 84%.^{17,18} EUS also is less reliable in determining the depth of invasion in lesions that have ulcerous changes, and EUS-based staging of ulcerated lesions should therefore be viewed with caution.¹⁹

Contrast-Enhanced Cross-sectional Imaging

Contrast-enhanced cross-sectional imaging—either computed tomography or magnetic resonance imaging—also should be a standard preoperative tool for the staging of gastric cancer. Specifically, contrast-enhanced images of the chest, abdomen, and pelvis typically are obtained to exclude the presence of distant disease, including hepatic and lung metastases, ascites, and omental involvement. They also will reveal the presence of bulky nodal disease. This finding should not preclude gastric resection; rather, it should alert the clinician to the likely possibility of advanced disease and/or the potential for undetected metastatic disease. However, cross-sectional imaging can understage gastric cancer in up to 25% of patients by missing peritoneal or sub-radiographic hepatic metastases.¹²

Positron emission tomography has emerged as an additional staging modality that can be used in combination with contrast-enhanced diagnostic computed tomography. Positron emission tomography currently is used to assess disease response to systemic therapy.²⁰

Diagnostic Laparoscopy

To overcome the previously mentioned limitations of contrast-enhanced imaging, diagnostic laparoscopy is

strongly recommended as an additional staging tool to avoid nontherapeutic laparotomy. Diagnostic laparoscopy permits examination of the diaphragm, liver, spleen, peritoneal lining, pelvis, small-bowel surface, and omentum for evidence of metastatic lesions. It is often performed in patients who have T3 or T4 gastric cancer without evidence of lymphadenopathy or distant metastases on computed tomography scans. Although patients who have T1 or T2 lesions often are treated with laparotomy and surgical resection without the use of diagnostic laparoscopy, diagnostic laparoscopy is strongly recommended as an additional staging tool in all stages of gastric cancer because it is more accurate than EUS or computed tomography.^{21,22}

The literature has shown that patients who underwent diagnostic laparoscopy began chemotherapy earlier by nearly half the time (19.5 vs 36.8 days, $P < .0001$) and had a reported shorter length of hospital stay (1.4 vs 6.5 days, $P < .05$) compared with patients who underwent laparotomy and were found to have unresectable/metastatic disease.^{23,24} Diagnostic laparoscopy can further upstage the disease of 25% to 48% of patients (sensitivity and specificity of 84% and 100%, respectively) who present with ostensibly resectable gastric cancer.^{23,25,26} At our institution, we use diagnostic laparoscopy liberally for patients with operable gastric cancer at the time of their surgery. We also use diagnostic laparoscopy in patients before the initiation of preoperative systemic therapy for operable gastric cancer and/or in those with linitis plastica. Additionally, diagnostic laparoscopy can be used to place a feeding tube in patients at risk for perioperative malnutrition.

Peritoneal lavage is an additional component of diagnostic laparoscopy that has been used to detect the presence of peritoneal metastatic disease owing to the fact that peritoneal spread is poorly predicted with computed tomography. The procedure is performed by instilling 500 mL of normal saline into the peritoneal cavity and allowing it to dwell therein for 10 minutes. The fluid is then aspirated via a suction trap assembly and sent for cytologic examination. Positive results of peritoneal cytology in the absence of other sites of metastatic disease (C1 disease) have been shown to correlate with a poor prognosis; patients with positive cytology have been shown to have a median survival of 14.8 to 20.0 months, compared with 98.5 months in those with negative cytology.^{27,28} However, peritoneal cytology can select out patients who initially have positive cytology (C1) for metastases but are later found to have negative cytology for metastases after neoadjuvant systemic therapy. These patients are reassessed with another peritoneal cytologic examination to identify those with conversion to negative cytology for spread (C0) after systemic therapy.²⁹ Conversely, peritoneal cytology also can select out up to 7% to 24% of

patients who are deemed to have C0 disease initially and receive neoadjuvant therapy but are found to have C1 disease at the time of repeat laparoscopy, thus sparing them an unnecessary laparotomy.^{27,30-32} At our institution, we have adopted a selective approach to peritoneal cytology during diagnostic laparoscopy. These scenarios include patients with linitis plastica or borderline performance status, and those with evidence of AJCC T4 disease on EUS or radiography.

Gastric Cancer Decision Making

A multidisciplinary strategy for the treatment of patients with newly diagnosed gastric adenocarcinoma is strongly recommended. The multidisciplinary approach is stage-dependent and should be implemented after the following steps regarding the patient, tumor, and treatment have been taken: (1) determining the patient's suitability to undergo gastrectomy; (2) obtaining the most reliable pre-therapy staging information to determine operability; and (3) determining the sequence of gastric cancer therapy (surgery first vs perioperative therapy).

Patient's Suitability to Undergo Gastric Cancer Surgery

When a patient is evaluated for surgical treatment, several factors should be considered before surgical resection is undertaken. The patient's underlying comorbidities, frailty, performance status, nutritional reserves, and electrolyte abnormalities all must be thoroughly evaluated. Although some comorbidities cannot be eliminated, they should be managed optimally before surgery. For example, preoperative malnutrition and electrolyte derangements should be corrected with preoperative total parenteral nutrition or supplemental nutrition.

Surgeons are occasionally faced with the dilemma of a patient who is both frail and in need of gastric cancer surgery. Emerging evidence points toward the potential beneficial effects on survival and quality of life of offering frail patients a short period of preoperative rehabilitation to optimize their operative course.^{33,34}

Reliable Pre-therapy Staging Information to Determine Operability

Obtaining appropriate staging information is crucial in determining a patient's operability. The combination of staging EUS, contrast-enhanced cross-sectional imaging, and diagnostic laparoscopy can provide the operating surgeon with reliable staging information to assess the potential for an R0 resection.

Sequence of Therapy

R0 gastrectomy and adequate lymphadenectomy are key components of operable gastric cancer therapy. The over-

all benefit is further improved with multimodal therapy (ie, systemic therapy with or without radiotherapy). As such, most patients with AJCC T2+ operable gastric cancer are offered either (1) surgery followed by adjuvant chemotherapy and/or chemoradiotherapy or (2) perioperative systemic therapy. There are 4 major clinical trials that have shown a survival advantage when multimodality therapy is integrated with gastrectomy. Each of these trials found that either postoperative therapy or perioperative (preoperative and postoperative) chemotherapy improved overall and disease-free survival. The trials are briefly mentioned here, and more details are discussed in other parts of this issue.

SWOG-9008/INT-0116. In 2001, SWOG-9008/INT-0116 (Southwest Oncology Group 9008/Intergroup Study 0116) compared patients with operable gastric cancer who underwent either a gastric resection alone or a gastric resection plus postoperative adjuvant chemotherapy (5-fluorouracil) and radiation (45 Gy, external beam). This US trial showed an improved 3-year overall survival rate (50% vs 41%) and disease-free survival rate (48% vs 31%) for the combination vs surgery alone.³⁵ The trial, however, has been criticized for a lack of adequate nodal dissection among its enrollees, especially given that 50% of them were found to have a D0 dissection. As such, critics feel that the observed survival benefit in the adjuvant therapy arm may represent patients with understaged node-positive disease who otherwise might have benefited from adjuvant therapy. Furthermore, the results of this trial do not mean that adjuvant therapy can compensate for inadequate gastric cancer surgery.

MAGIC trial. In 2006, the MAGIC (Medical Research Council Adjuvant Gastric Infusional Chemotherapy) trial evaluated the use of perioperative chemotherapy (ie, neoadjuvant and adjuvant) in patients with operable gastric cancer. This trial reported a higher 5-year survival rate with perioperative chemotherapy (epirubicin, cisplatin, and fluorouracil) than with surgery alone (36% vs 23%); progression-free survival also was improved.³⁶

CLASSIC study. The CLASSIC (Capecitabine and Oxaliplatin Adjuvant Study in Stomach Cancer) study is an Asian trial from 2012 that evaluated adjuvant chemotherapy with capecitabine and oxaliplatin following gastrectomy and D2 lymphadenectomy. After 34 months, this trial showed improved 3-year disease-free survival with chemotherapy plus surgery vs surgery alone (74% vs 59%).³⁷ Although this was a significant increase in survival compared with the SWOG-9008/INT-0116 and MAGIC trials, many have noted that because the study is from Asia, the results may be attributable to different tumor biology and surgical expertise.³⁸

ARTIST trial. No large trials evaluated postoperative chemoradiotherapy after gastric resection in the decade following SWOG-9008/INT-0116. Then, in 2012, the ARTIST (Adjuvant Chemoradiation Therapy in Stomach Cancer) trial evaluated patients who underwent gastrectomy with D2 lymphadenectomy; patients were randomly assigned to chemotherapy alone or to chemotherapy plus radiotherapy. The results showed no significant increase in disease-free survival with the addition of radiotherapy, and only a slight improvement in 3-year disease-free survival was found in a subgroup analysis (74% for chemotherapy only vs 78% for chemotherapy/radiotherapy). The authors concluded that the addition of radiotherapy did not significantly reduce recurrence after resection. A subsequent trial is planned to evaluate radiotherapy in patients with lymph node–positive gastric cancer.³⁹

Our recommendations for the sequence of multimodal therapy, based on these trials, depend on the biology of the tumor. Preoperative chemotherapy is recommended when it can lead to better R0 resection. At our institution, when planning treatment strategy, we consider the presence of linitis plastica and location of the tumor. For example, patients who have proximal gastric cancers typically have less favorable survival outcomes overall and require more complex resections (total vs subtotal gastrectomy) with perioperative systemic therapy. Those who have distal gastric tumors, however, typically present with tumor-related events (eg, bleeding, obstruction); this presentation favors a surgery–first approach and typically carries a better outcome.

Gastrectomy: Summary of Operative Techniques

Margin-negative gastrectomy and adequate lymphadenectomy are the cornerstones of the treatment for operable gastric cancer. Because the extent of gastric resection largely depends upon tumor location within the stomach, the most common types of gastric cancer resection are total gastrectomy, subtotal gastrectomy, and esophago-gastrectomy. We perform total gastrectomy for proximal gastric cancer, total or subtotal gastrectomy for tumors of the middle third, and subtotal gastrectomy for cancers of the distal third. For tumors involving the GE junction, margin-negative esophagectomy is additionally required.

Total Gastrectomy

Patients with proximal gastric cancers not involving the GE junction (ie, cancers of the cardia or fundus) usually undergo total gastrectomy. This involves removal of the entire stomach, including the GE junction and omentum, and subsequent intestinal restoration with a Roux-en-Y reconstruction (Figure 1). The surgeon first

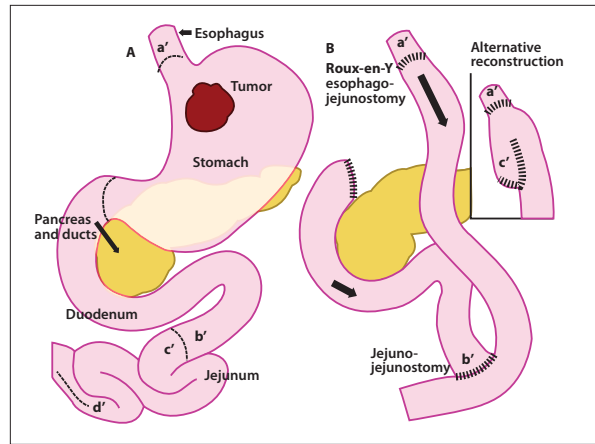


Figure 1. Total gastrectomy and Roux-en-Y esophagojejunal reconstruction.

carefully dissects the stomach and mobilizes it, freeing it of all attachments, before ligating the pertinent feeding vessels. Finally, the surgeon transects the stomach just above the duodenum and below the distal esophagus. The surgeon also resects all of the gastric arteries at their origin.¹¹ Intraoperative frozen section evaluation is used to ensure normal duodenal and esophageal mucosa.

Subtotal Gastrectomy

Tumors of the mid body and distal tumors usually are resected with a subtotal gastrectomy (Figure 2). The technique is similar to that for total gastrectomy; however, only approximately 70% to 80% of the distal stomach is removed while negative resection margins (ie, 4- to 6-cm negative proximal margins and 2-cm negative distal margins) are ensured. As with total gastrectomy, the operating surgeon should ligate all of the gastric arteries at their origin. However, the short gastric vessels should be preserved to avoid gastric remnant ischemia. We prefer a Roux-en-Y gastrojejunal reconstruction (Figure 2) over loop gastrojejunostomy in order to minimize bile reflux to the gastric remnant.¹¹

Studies comparing total vs subtotal gastrectomy have shown no significant difference in overall or disease-free survival between these surgical approaches for distal gastric cancer. The 5-year overall survival rate is 41% for total gastrectomy and 43% for subtotal gastrectomy.⁴⁰ Subtotal gastrectomy has been associated with better nutritional outcomes and better quality of life when compared with total gastrectomy.⁴¹

Esophagectomy

Proximal tumors have been increasing in the United States, despite decreasing rates of gastric cancer in Western countries.⁴⁰ Proximal tumors have been described based on the Siewert classification scheme: type 1, in which the tumor

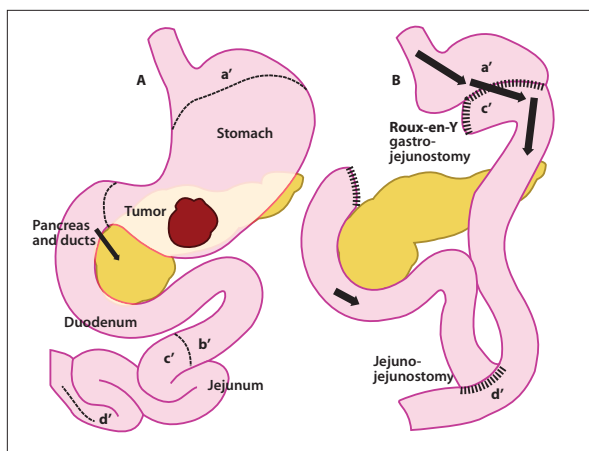


Figure 2. Subtotal gastrectomy and Roux-en-Y gastrojejunostomy reconstruction.

center is 1 to 5 cm proximal to the GE junction; type 2, in which the tumor center is 1 cm proximal and 2 cm distal to the GE junction; and type 3, in which the tumor center is 2 to 5 cm distal to the GE junction.^{11,40} Patients with proximal tumors usually require an esophagectomy or extended gastrectomy, with the stomach or jejunum used for intestinal continuity.

Additional Procedures

Lymphadenectomy

Lymphadenectomy with adequate histopathologic nodal evaluation is an important component of staging and therapy in patients undergoing surgical treatment for gastric cancer.⁴² The extent of lymphadenectomy has been one of the most controversial areas in gastric cancer treatment. There are 4 types of lymphadenectomy (Figure 3): D0, which refers to incomplete and inadequate node dissection and should be reserved for surgical palliation only; D1, which refers to resection of the perigastric lymph nodes; D2, which refers to D1 plus resection of the nodes surrounding the celiac trunk, along with distal pancreatectomy and splenectomy; and D3, which refers to D2 plus resection of the nodes from the celiac axis to the inferior mesenteric artery.⁴³

Most trials from Asia have supported the use of more extensive lymphadenectomy (D2 or D3).⁴⁴ They have reported more favorable 5-year survival rates in comparison with the West.⁴⁵ Conversely, earlier Western studies have shown no additional survival benefits in the cohorts with extended lymphadenectomy, and the rates of operative complications were higher in patients who underwent D2 lymphadenectomy.⁴⁶ The most notable of the Western studies are the Dutch Gastric Cancer Group (DGCG) trial and the British Medical Research Council (MRC) ST01 trial. The DGCG trial evaluated patients

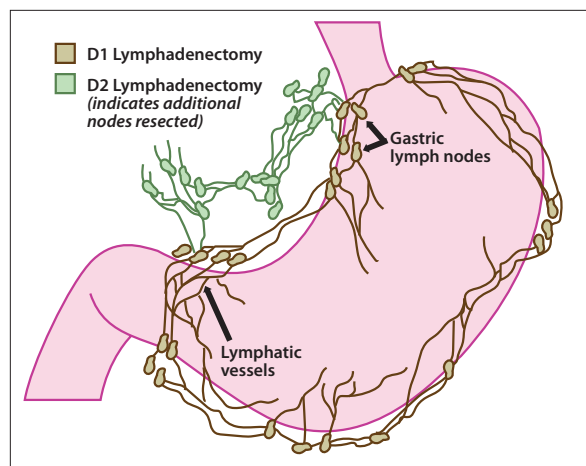


Figure 3. D1 and D2 lymphadenectomy. The brown nodes illustrate a D1 lymphadenectomy, with resection of the perigastric lymph nodes. The green nodes illustrate a D2 lymphadenectomy, with extended resection of the nodes surrounding the celiac artery; the splenectomy and distal pancreatectomy are not shown.

who underwent D1 or D2 lymphadenectomy and concluded that compared with D1 lymphadenectomy, D2 lymphadenectomy had a higher operative mortality (4% for D1 vs 10% for D2) and surgical complication rate (25% for D1 vs 43% for D2), with no statistically significant increase in 5-year overall survival seen for D2 (45% for D1 vs 47% for D2).⁴⁷ Furthermore, the MRC trial, which was performed in the United Kingdom, supported the results of the DGCG trial. There was no statistically significant difference between the 5-year overall survival rate with D1 (35%) and that with D2 (33%). This led to the conclusion that the classic Japanese D2 resection offered no survival benefit over the D1 resection.⁴⁸

A more recent randomized trial by the Italian Gastric Cancer Study Group supported the results of previous Western studies that found no notable survival benefit for D2 over D1 lymphadenectomy. The 5-year overall survival rate was 66.5% with D1 vs 64.2% with D2 ($P=.695$). However, subgroup analysis suggested that D2 lymphadenectomy may be a better choice for patients with advanced disease (AJCC T2-T4) noted preoperatively.⁴⁹ In 2015, a Cochrane meta-analysis examined 8 Asian and European lymphadenectomy trials including more than 2500 patients and found no significant difference between D1 and D2 lymphadenectomy in regard to overall and disease-free survival. However, further analysis showed significantly improved disease-specific survival when D2 was compared with D1 lymphadenectomy, although there were higher operative mortality rates in the D2 lymphadenectomy groups.⁵⁰

All of these studies compared D1 with D2 lymphadenectomy, whereas 2 other prominent studies evaluated

the number of lymph nodes resected and the effect on overall survival. The first study, by Smith and colleagues, noted a greater survival difference when more than 10 lymph nodes were resected, and a continued survival difference when up to 40 lymph nodes were examined. These findings support a potential therapeutic role for extended lymphadenectomy in patients undergoing curative gastrectomy.⁵¹ A more recent study, by Datta and colleagues, has now recommended that a total yield of at least 15 lymph nodes be examined for an adequate lymphadenectomy during gastric resection. In their analysis, an inadequate lymphadenectomy (<15 lymph nodes examined) was independently associated with worse overall survival.^{7,52} This worse overall survival has also been noted by others and has supported the goal of examining at least 15 lymph nodes to classify a lymph node dissection as adequate.⁷

Many have suggested that the controversy between Asian and Western lymphadenectomy outcomes is likely attributable to differences in disease biology, surgical expertise, and body mass index.^{53,54} Based on the current level of evidence, at least a D1 lymphadenectomy with a total nodal yield of 15 or more lymph nodes is recommended as part of adequate gastric cancer surgery.

Minimally Invasive Gastrectomy

Recently, minimally invasive gastrectomy has been introduced into the armamentarium of gastric cancer surgery. Studies have shown that minimally invasive gastrectomy is associated with decreased incisional pain, length of stay, use of narcotics, and complication rates.⁵⁵⁻⁵⁸ Although current evidence suggests that minimally invasive gastrectomy is beneficial, most of the studies have included patients with smaller tumors. This important caveat should be noted when minimally invasive gastrectomy is compared with open gastric cancer surgery performed for larger and more advanced gastric cancers.^{58,59} The adoption by surgeons of minimally invasive gastrectomy for cancer remains to be assessed.

Endoscopic Mucosal Resection

Endoscopic mucosal resection for gastric malignancies is an emerging technique in the Western setting. It involves the endoscopic resection of early-stage gastric cancers with the following favorable criteria: (1) size of less than 2 cm; (2) moderately or well-differentiated histopathology; (3) clear lateral and deep resection margins; (4) absence of penetration through the superficial submucosa; and (5) absence of lymphovascular invasion.^{60,61} We speculate that endoscopic mucosal resection has not been fully adopted in the United States owing to its operator dependency, additional level of expertise needed, and lack of level 1 evidence in the West.⁶⁰

Survival Outcomes

Gastric cancer carries a 5-year overall survival rate of approximately 20% to 30% in Western populations, in which most patients present with advanced-stage disease.³ According to data from the US National Cancer Data Base (NCDB), up to 65% of patients with gastric cancer had advanced disease (T3/T4) and 85% of these patients harbored nodal metastases at the time of diagnosis.¹¹ Patients who were treated surgically with curative intent had a median survival of 24 months (5-year survival rate, 20%-30%). In contrast, patients who underwent palliative treatment and those who had no gastric cancer therapy had median survivals of 8 and 5.4 months, respectively.¹¹ Through further analysis of Western survival data, the Memorial Sloan Kettering Cancer Center has created an externally validated nomogram that estimates the survival of a patient with gastric cancer after a complete surgical resection and can be used to help inform a patient's postoperative likelihood of survival.^{62,63}

Surgical Outcomes

The overall operative mortality after gastric cancer surgery, especially total gastrectomy, is relatively low (<2%) when the procedure is performed at high-volume centers.⁶⁴ Owing to the relationship between hospital volume and operative outcomes at up to 1 year, the 30-day mortality rate declined from 4.5% to 2.3% and the 90-day mortality rate declined from 6.9% to 4.5%, according to the United Kingdom's National Oesophago-Gastric Cancer Audit (NOGCA).⁶⁵

Despite the low operative mortality rate, operative complications after gastric cancer surgery approach 30% to 40%.⁶⁶ For example, total gastrectomy is associated with several complications, ranging from those that are systemic (pulmonary embolism, pneumonia, myocardial infarction, deep vein thrombosis) to more technically related complications (anastomotic leak, anastomotic stricture). Additionally, the rate of readmissions after gastrectomy has been estimated to range from 7% to 20%, and readmissions are most commonly due to gastrointestinal complications.^{67,68}

Predictors of poorer long-term outcomes of gastric cancer include proximal location of the gastric cancer, older age, greater intraoperative blood loss, receipt of perioperative blood transfusions, AJCC T3-4 disease, AJCC N+ disease, features of signet ring cell carcinoma, and R1/R2 resection (resection margins with microscopic or gross residual disease).^{69,70}

Palliation

Because 30% of patients who have gastric cancer present with locally advanced or stage IV disease, surgeons

often are asked to render an opinion regarding surgical palliation (eg, resection or bypass). These palliative decisions are typically complicated and should be considered in conjunction with (1) the patient's underlying performance status, (2) the patient's life expectancy, and (3) the predicted or actual degree of success with nonsurgical palliative options, such as stenting and radiotherapy. The goal should be to offer surgical palliation without negatively impacting quality of life.^{71,72} Because of the risk for operative mortality and morbidity, palliative surgical interventions should be thoroughly discussed with patients and their families.

Surveillance

In line with the current recommendations of the National Comprehensive Cancer Network, patients who have undergone gastric resection should be followed every 3 to 6 months for the first 2 years after their operation. The surveillance strategy should include a routine history and physical examination, upper gastrointestinal endoscopy (for those who have not undergone a total gastrectomy), and cross-sectional computed tomography. Laboratory tests should include a complete blood cell count, a basic metabolic panel, liver function tests, and measurement of the levels of vitamin B₁₂, vitamin D, prealbumin, and iron. The surveillance intervals can be extended to every 6 to 12 months after 2 years provided there is no evidence of recurrence.⁶¹

Conclusion

Gastric cancer is the third leading cause of cancer-related deaths worldwide, with rates that vary depending on geographic location. Margin-negative gastrectomy and adequate lymphadenectomy (removal of ≥ 15 lymph nodes) are the cornerstone elements of a multimodal treatment approach for operable gastric cancer. Diagnostic laparoscopy should be included in the management armamentarium for newly diagnosed gastric cancer to overcome the limitations of cross-sectional imaging in identifying sub-radiographic hepatic or peritoneal metastases. The benefit of surgical therapy is enhanced by at least 13% when it is integrated with multimodality therapy in either of 2 sequences (surgery first followed by adjuvant chemoradiotherapy or perioperative systemic therapy).^{35,36} The multidisciplinary approach to treatment will continue to be an evolving paradigm, especially with the emergence of systemic and targeted therapies.

Disclosures

The authors have no relevant financial disclosures to make.

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