Surgical Treatment for Gastric Cancer

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KEYWORDS

• Gastric cancer • Gastrectomy • Lymphadenectomy • Staging laparoscopy

KEY POINTS

- Staging laparoscopy is an important modality for patients with gastric cancer with stages T1b or greater to evaluate for peritoneal spread when chemoradiation or surgery is considered.
- The appropriate surgical procedure for gastric cancer is based on the lesion's location: subtotal gastrectomy is generally the procedure of choice for distal tumors, whereas total gastrectomy is generally performed for proximal lesions in the upper third of the stomach.
- D2 lymphadenectomy is now supported as a critical part of a curative intent resection given that gastric cancer spreads through lymphatics to regional lymph nodes.

Video content accompanies this article at http://www.giendo.theclinics.com.

INTRODUCTION

Regionality is an important theme when it comes to the surgical management of gastric cancer. Not only does the location of gastric cancer and its extent of spread dictate the operative plan but also, historically, the management of gastric cancer is often thought of in terms of "Eastern versus Western" approaches. Incidence rates in Eastern Asia are significantly higher than they are in North America.[1] The greater experience in treating gastric cancer in Asian institutions has led to differing management practices in terms of screening and prevention as well as in treatment.[2] In terms of surgical management, Eastern surgeons have been pioneers and proponents of minimally invasive techniques and more extensive lymph node dissections, which have been controversial in Western institutions but are now being performed with greater frequency. Despite some ongoing debate about the details of gastric cancer management, what is agreed on is that surgery is an essential component of

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curative-intent treatment strategies. However, the care of each patient with gastric cancer must be individualized and may require additional neoadjuvant or adjuvant therapies, such as chemotherapy or radiation therapy. With the ongoing development of new therapeutics, such as immunotherapy, and technologies, such as robotic surgery, the future of gastric cancer care will continue to evolve and require the coordinated teamwork of physicians with different medical and surgical expertise to optimize patient outcomes. It is important that all physicians who will be caring for patients with gastric cancer understand the current best practices of surgical management to provide patients with the highest quality of care. This article aims to provide this information while acknowledging areas of surgical management that are still controversial.

STAGING LAPAROSCOPY AS PART OF THE STAGING EVALUATION

Conventional staging for gastric cancer usually includes a physical examination, a computed tomographic (CT) scan of the chest/abdomen/pelvis, and an endoscopic ultrasound, which is performed in accordance with the TNM staging system of the combined American Joint Committee on Cancer/Union for International Cancer Control (**Table 1**).[3] Per National Comprehensive Cancer Network (NCCN) guidelines, the performance of a staging laparoscopy with peritoneal washings is also indicated for clinical stages $\geq$T1b to evaluate for peritoneal spread when chemoradiation or surgery is considered.[4] Many experts follow these guidelines and support its use for locally advanced disease and for patients being considered for neoadjuvant therapy but not for those with early-stage disease.[5] A staging laparoscopy is performed to directly visualize the liver surface, peritoneum, and lymph nodes while allowing for the biopsy of any worrisome lesions and the collection of peritoneal fluid for cytologic analysis. Staging laparoscopy, with reported sensitivity of 86% and specificity of 100%, is superior to radiographic studies for detecting metastatic disease and may detect radiographically occult disease that can alter management in approximately 9% to greater than 50% of patients with only localized disease on imaging.[6–9] If metastatic disease is identified, a patient may be spared from the performance of an unnecessary laparotomy, which has a morbidity of 13% to 23% and a mortality of 10% to 21%, whereas staging laparoscopy has a morbidity of 0% to 2.5% and no reported mortality.[7,10–13] During laparoscopy, peritoneal fluid can be collected and sent for cytology, which if positive, upstages a patient to stage IV disease and is a poor prognostic sign predictive of disease recurrence.[9,14] Studies are ongoing to further delineate the role of surgery and neoadjuvant strategies for individuals with positive cytology.[15,16]

When a patient is selected to undergo staging laparoscopy, it can be performed as a one- or a 2-stage approach. In a one-stage approach, the staging laparoscopy is performed concurrently at the same time as the planned surgical resection. In a 2-stage approach, the staging laparoscopy is the only procedure performed to be followed at a later date by a separate surgical resection if no metastatic disease is identified during the staging laparoscopy. The advantage of the one-stage approach is that it involves only 1 procedure and 1 anesthetic exposure. However, the disadvantage is that it can add additional time and complexity to the case if there is uncertainty with a frozen section biopsy or if there is a need for final pathology to confirm a worrisome finding. It is also not possible to have cytology examined during a one-stage procedure. The advantage of performing the staging laparoscopy separately in a 2-stage approach is that it may identify patients who are more suited for a neoadjuvant approach. Although a 2-stage approach requires the patient to be exposed a second time to anesthesia for a definitive cancer operation, it is a more robust approach for ensuring

Table 1
Eighth American Joint Committee on Cancer staging system for gastric adenocarcinoma

Primary tumor	TX	Primary tumor cannot be assessed		
	T0	No evidence of primary tumor		
	Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria, high-grade dysplasia		
	T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa		
	T1a	Tumor invades the lamina propria or muscularis mucosae		
	T1b	Tumor invades the submucosa		
	T2	Tumor invades the muscularis propria		
	T3	Tumor penetrates the subserosal connective tissue without invasion of the visceral peritoneum or adjacent structures		
	T4	Tumor invades the serosa (visceral peritoneum) or adjacent structures		
	T4a	Tumor invades the serosa (visceral peritoneum)		
	T4b	Tumor invades adjacent structures/organs		
Regional nodes	NX	Regional lymph nodes cannot be assessed		
	N0	No regional lymph node metastasis		
	N1	Metastasis in 1 or 2 regional lymph nodes		
	N2	Metastasis in 3 to 6 regional lymph nodes		
	N3	Metastasis in 7 or more regional lymph nodes		
	N3a	Metastasis in 7 to 15 regional lymph nodes		
	N3b	Metastasis in 16 or more regional lymph nodes		
Metastases	M0	No distant metastasis		
	M1	Distant metastasis		
Stage groupings (pathologic)	0	TisN0M0	IIIB	T1N3bM0
	IA	T1N0M0		T2N3bM0
	IB	T1N1M0		T3N3aM0
		T2N0M0		T4aN3aM0
	IIA	T1N2M0		T4bN1M0
		T2N1M0		T4bN2M0
		T3N0M0	IIIC	T3N3bM0
	IIB	T1N3aM0		T4aN3bM0
		T2N2M0		T4bN3aM0
		T3N1M0		T4bN3bM0
		T4aN0M0	IV	Any T, any N, M1
	IIIA	T2N3aM0		
		T3N2M0		
		T4aN1M0		
		T4aN2M0		
		T4bN0M0		

From Cameron J and Cameron A 2019. Current surgical therapy. 13th edition. p.102.

accurate staging. As the role of staging laparoscopy continues to be defined, it remains underused in the United States: 1 study suggested that it was only performed in 8% of older patients with gastric cancer.[17]

The uptake is likely higher at major cancer centers, where staging laparoscopy is acknowledged as an important aspect of accurate staging.[18] As further research elucidates the value of neoadjuvant approaches and as more surgeons learn of its utility, there may be a greater uptake of staging laparoscopy to rule out metastatic disease and to obtain cytology to guide specific therapy (Video 1).

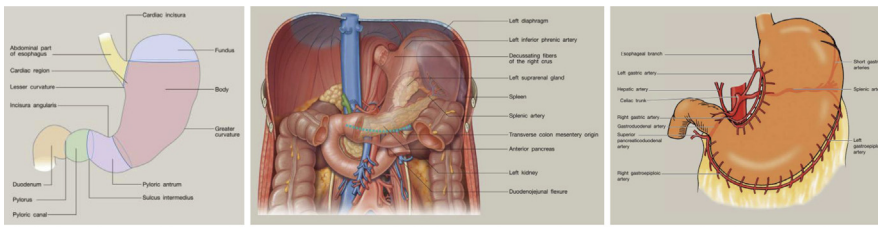
SURGICAL APPROACH

Anatomy

Knowledge of the surgical anatomy of the stomach is important not only for the technical performance of gastric cancer surgery but also to help all providers understand the physiologic changes that may be seen in patients after gastrectomy. **Fig. 1** shows the important anatomic structures and the relevant blood supply. Located in the left upper quadrant of the abdomen, the stomach is adjacent to many important structures, including the left lateral lobe of the liver, the transverse colon, omentum, pancreas, spleen, left kidney, left adrenal gland, and the diaphragm. The stomach can be divided into 5 anatomic sections based on histology and function: (1) cardia and gastroesophageal junction, (2) fundus, (3) body, (4) antrum, and (5) pylorus. The cardia, the proximal stomach next to the lower esophageal sphincter, contains mucus and endocrine cells. The fundus, adjacent to and rising above the cardiac opening, contains parietal cells, chief cells, endocrine cells, and mucus cells. The body, between the fundus and antrum, contains cells similar to the fundus. The antrum, the distal stomach separated from the body by the angular incisura, contains pyloric glands, endocrine cells, mucus cells, and G cells. The pyloric sphincter, a muscular valve separating the antrum from the duodenum, contains mucus cells and endocrine cells. The lesser curve of the stomach is supplied by the left and right gastric arteries, which branch off the celiac and common hepatic arteries, respectively. The greater curvature is supplied by the right and left gastroepiploic arteries, which arise from the gastroduodenal and splenic arteries, respectively. The fundus of the stomach is supplied by the short gastric arteries, which also come off the splenic artery. Veins parallel the arterial supply.[19,20] The lymph node stations of the stomach have been defined by the Japanese Research Society for the Study of Gastric Cancer and are grouped into 16 stations according to location: 1 to 6 are perigastric and the others are adjacent to major blood vessels, along the aorta, or behind the pancreas.[21] **Table 2** contains description of the lymph node stations.

Indicators of Resectability

Resection offers patients with gastric cancer the best chance for cure, but patients must be appropriately referred for what can be a major procedure. Patients being considered for resection must not have severe comorbidities that would prevent the safe receipt of anesthesia. A gastric cancer is generally considered unresectable if there are distant metastases, invasion of major vasculature such as the aorta, or encasement of the hepatic artery or celiac axis. Involvement of the distal splenic artery



The borders and regions of the stomach | Posterior topographical relations of the stomach | Arterial supply of the stomach

Fig. 1. Stomach anatomy and vasculature. (*From* Vishy Mahadevan, Anatomy of the stomach, Surgery (Oxford), Volume 35, Issue 11, 2017, Pages 608-611, ISSN 0263-9319, https://doi.org/10.1016/j.mpsur.2017.08.004. Accessed via https://www.sciencedirect.com/science/article/pii/S0263931917301850.)

Table 2
Anatomic definitions of lymph node stations

No.	Definition
1	Right paracardial lymph nodes (LNs), including those along the first branch of the ascending limb of the left gastric artery
2	Left paracardial LNs, including those along the esophagocardiac branch of the left subphrenic artery
3a	Lesser curvature LNs along the branches of the left gastric artery
3b	Lesser curvature LNs along the 2nd branch and distal part of the right gastric artery
4sa	Left greater curvature LNs along the short gastric arteries (perigastric area)
4sb	Left greater curvature LNs along the left gastroepiploic artery (perigastric area)
4d	Right greater curvature LNs along the 2nd branch and distal part of the right gastroepiploic artery
5	Suprapyloric LNs along the 1st branch and proximal part of the right gastric artery
6	Infrapyloric LNs along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreatoduodenal vein
7	LNs along the trunk of left gastric artery between its root and the origin of its ascending branch
8a	Anterosuperior LNs along the common hepatic artery
8p	Posterior LNs along the common hepatic artery
9	Celiac artery LNs
10	Splenic hilar LNs, including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1st gastric branch
11p	Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end
11d	Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail
12a	Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12b	Hepatoduodenal ligament LNs along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12p	Hepatoduodenal ligament LNs along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
13	LNs on the posterior surface of the pancreatic head cranial to the duodenal papilla
14v	LNs along the superior mesenteric vein
15	LNs along the middle colic vessels
16a1	Paraaortic LNs in the diaphragmatic aortic hiatus
16a2	Paraaortic LNs between the upper margin of the origin of the celiac artery and the lower border of the left renal vein

(*continued on next page*)

Table 2
(continued)

No.	Definition
16b1	Paraaortic LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery
16b2	Paraaortic LNs between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation
17	LNs on the anterior surface of the pancreatic head beneath the pancreatic sheath
18	LNs along the inferior border of the pancreatic body
19	Infradiaphragmatic LNs predominantly along the subphrenic artery
20	Paraesophageal LNs in the diaphragmatic esophageal hiatus
110	Paraesophageal LNs in the lower thorax
111	Supradiaphragmatic LNs separate from the esophagus
112	Posterior mediastinal LNs separate fro

Adapted from Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 14, 101–112 (2011). https://doi.org/10.1007/s10120-011-0041-5.

is not a contraindication to resection, as the vessel can be taken en bloc along with the stomach, spleen, and distal pancreas. The presence of bulky lymph nodes in the aortocaval region, mediastinum, or the porta hepatis is considered distant disease and is classified as stage IV.[6] Concerning linitis plastica, extensive tumor infiltration of the stomach resulting in a rigid thickened stomach, which is associated with poor prognosis, there is some controversy as to whether this should be considered resectable or not; however, in the era of neoadjuvant therapy, many surgeons would elect to proceed with resection if negative margins can be obtained.[22–24] Of note, although patients with metastatic gastric cancer generally are not eligible for curative surgery, this does not mean that these patients are excluded from surgical treatments, which may be of benefit to some patients with complications, such as obstruction, bleeding, or perforation (see later section on Palliative Interventions).

Preoperative Planning

The decision to pursue gastric cancer resection should occur with consultation of a multidisciplinary tumor board to ensure that an appropriate multimodality treatment strategy is planned. In the United States, neoadjuvant therapy is advocated by NCCN guidelines and is increasingly pursued before surgical resection.[4] Furthermore, given that most resections will be performed under elective situations, it is critical for patients to undergo preoperative medical assessments, as most of these patients are older and present with comorbidities.[25] As part of the workup, genetic counseling may be indicated in cases whereby any genetic syndrome, such as hereditary diffuse gastric cancer, familial adenomatous polyposis, or Peutz-Jeghers, is suspected.[26] During the consent process for surgery, patients should be made aware not only of the risks of surgery and its complications but also of complications related to anesthesia, the possibility of a prolonged intensive care unit course, and the potential need for additional therapies, such as chemotherapy or radiation depending on the surgical pathology.[27] Before surgery, some surgeons will give patients a mechanical bowel preparation or antibiotics for oral enteral decontamination, but there currently are not enough data to support these practices as routine.[28,29] At the time of surgery, patients will receive antibiotic and venous thromboembolism prophylaxis.

Total versus Partial Gastrectomy

Although endoscopic resection is proving to be a promising technique for early cancers, surgical gastrectomy remains the most frequently performed procedure for the treatment of invasive gastric cancer. Currently, there are 2 main approaches that can be used based on the gastric cancer's location and characteristics: total gastrectomy and partial gastrectomy, which is a broad term referring to any procedure not removing the entire stomach (**Fig. 2**). It is important to note that these procedures are sometimes performed for reasons outside of gastric cancer. However, in the setting of gastric cancer, they must be performed adhering to oncologic principles, including attention to surgical margins and appropriate lymph node dissection. As such, for gastric adenocarcinoma in the distal stomach, smaller resections, such as wedge resections or distal gastrectomy, generally are not appropriate, as they do not allow for adequate lymphadenectomy.[6] Subtotal gastrectomy, in which only the fundus of the stomach is retained, is required to ensure the lymph nodes of the lesser curvature are fully removed, and only well-vascularized viable stomach is remaining because the ligation of the left gastric artery is required for a proper lymph node dissection. Total gastrectomy, the removal of the entire stomach, is generally performed for proximal lesions in the upper third of the stomach. Although proximal gastric cancers can technically be approached with either a total gastrectomy or a proximal partial gastrectomy, total gastrectomy is currently preferred because it is associated with a much lower rate of reflux esophagitis when performed with a Roux-en-Y reconstruction (2% vs >30%), a more complete lymph node dissection, and fewer complications.[30,31] However, the preference for total over proximal partial gastrectomy is based on older data, and there are ongoing studies to further evaluate these approaches (randomized clinical trial ongoing, KLASS 05 trial).[32] Regarding distal tumors, the literature has shown that there is no added survival benefit for total gastrectomy compared with subtotal gastrectomy, which is why the latter less aggressive approach is preferred.[33,34] In some cases of local invasion, the removal of adjacent organs may also be needed in order to perform a curative intent procedure.

The general surgical steps involved in partial or total gastrectomy include the following (Video 2):

1. Mobilization of the greater curvature with division of the left gastroepiploic. The short gastric vessels are also divided for total gastrectomy, and omentectomy is considered for advanced cancers.[35]
2. Infrapyloric mobilization with ligation of the right gastroepiploic vessels

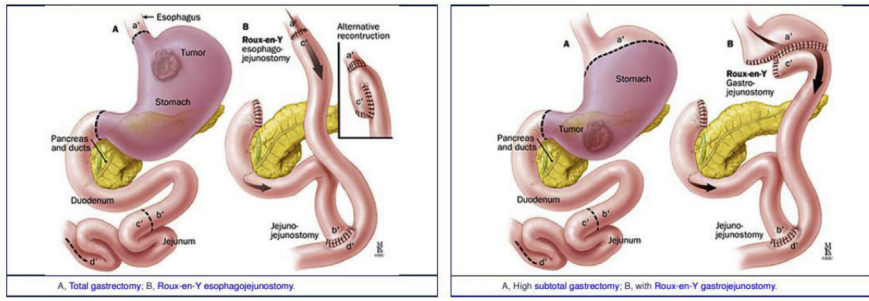


Fig. 2. Total versus subtotal gastrectomy. (Illustrations by Michael Linkinhoker © 2013 Johns Hopkins University. All rights reserved)

3. Suprapyloric mobilization with ligation of the right gastric vessels
4. Duodenal transection
5. D2 or D1+ lymphadenectomy, with dissection of the porta hepatis, common hepatic artery, left gastric artery, celiac axis, and splenic artery, and ligation of left gastric vessels (based on location)
6. Gastric (or esophageal) transection
7. Reconstruction by loop or Roux-en-Y gastrojejunostomy (or Roux-en-Y esophagojejunostomy)[36]

When preparing patients for total gastrectomy, it is important to prepare and drape the chest in addition to the abdomen because of the possibility of needing to perform a thoracotomy to obtain a clear proximal margin. For both procedures, intraoperative frozen sections are generally performed to ensure that the cancer is fully removed. Regarding partial gastrectomy, there are some variations developed by the Japanese that are sometimes performed to limit postoperative syndromes that result from altered gastric anatomy and physiology (see later discussion under Complications).[37–40] Function-preserving techniques include those that preserve the pylorus (pylorus-preserving segmental gastrectomy) and those that preserve the distal named branches of the vagus nerves.[37–40] These techniques are not widely described in North American literature.

Optimal Surgical Margin

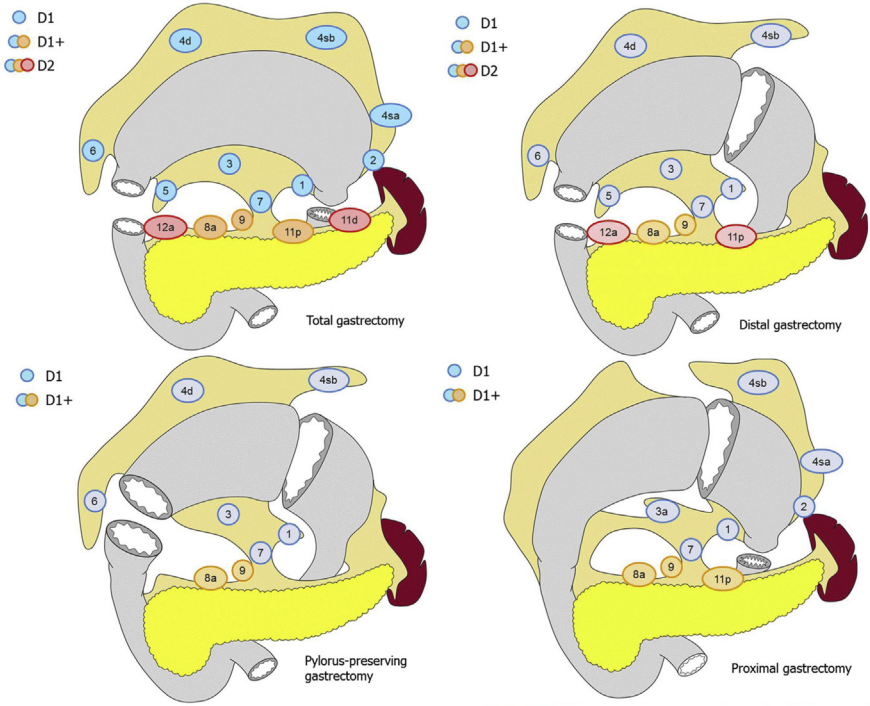
The goal of gastric resection for adenocarcinoma is to obtain a tumor-free resection margin (R0) on pathologic examination because positive margins have been associated with worse outcomes.[41] Another consideration is that gastric cancer has a tendency for intramural spread.[42] Although it was previously thought that a gross margin of at least 5 cm was needed to obtain an R0 resection, this was based on older data, and thus, there is ongoing debate as to the optimal margin, particularly in light of increased use of neoadjuvant chemotherapy before resection.[6] NCCN guidelines previously endorsed obtaining a margin $\geq$4 cm from the gross tumor, but now they simply recommend "adequate gastric resection to achieve negative microscopic margins."[4] Although there are no randomized data to guide margin management, retrospective studies have been performed and have suggested obtaining margins ranging from 2 to 6 cm.[43,44] The 2018 Japanese Gastric Cancer Treatment Guidelines recommend a gross resection margin of 2 cm for T1 tumors, 3 cm margin for T2 or deeper tumors with an expansive growth pattern, and 5 cm for T2 or deeper tumors with an infiltrative growth pattern.[45] Ultimately, the operating surgeon must determine the appropriate margin considering whether the risk of morbidity from further resection outweighs the potential oncologic benefit. To identify whether the margin is adequate, intraoperative frozen sections of the proximal and distal margins should be obtained in all patients undergoing potentially curative surgery. Based on the results of these frozen sections, a wider excision may be necessary, as improved outcomes have been reported with successful reexcision.[46] However, experts recognize that it may be difficult to obtain a negative margin even with successive frozen sections.[47] There is no gold standard of care when it comes to positive frozen section margins, and management is currently surgeon and institution dependent.

Extent of Lymph Node Dissection

Given that gastric cancer spreads through lymphatics to regional lymph nodes, curative intent resections must focus on adequate control of the lymph nodes for staging, minimizing recurrence, and improving overall survival. The 16 lymph node stations

defined by the Japanese Research Society for the Study of Gastric Cancer have been grouped into a broader classification scheme that is used to describe the extent of lymph node dissection based on the nodal stations to be removed. The extent of lymphadenectomy is categorized into D1, D1+, D2, or D3, ranging from the minimal required lymph nodes to a more extensive lymph node dissection. A D3 lymphadenectomy is referred to as a superextended lymphadenectomy and includes a D2 lymphadenectomy plus the removal of nodes within the root of mesentery and periaortic regions (stations 1–16). The nodal stations that make up each lymph node removal degree are defined by the type of gastrectomy conducted, which is in turn driven by the location of the tumor (**Fig. 3**).[6,45]

The extent of lymph node dissection (D1 vs D2 vs D3) needed during a gastric cancer resection has been a topic of controversy. In Eastern countries, D2 lymphadenectomy is considered standard of care. Western institutions have also started to adopt



	D0	D1	D1+	D2
Total Gastrectomy	Lymphadenectomy less than D1	No. 1-7	D1 + No. 8a, 9, 11p	D1 + No. 8a, 9, 11p, 11d, 12a
Distal Gastrectomy	Lymphadenectomy less than D1	No. 1, 3, 4sb, 4d, 5, 6, 7	D1 + No. 8a, 9	D1 + No. 8a, 9, 11p, 12a
Pylorus-preserving gastrectomy	Lymphadenectomy less than D1	No. 1, 3, 4sb, 4d, 6, 7	D1 + No. 8a, 9	
Proximal gastrectomy	Lymphadenectomy less than D1	No. 1, 2, 3a, 4sa, 4sb, 7	D1 + No. 8a, 9, 11p	

Fig. 3. Lymph node stations. (*From* Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018, 5th edition. Gastric Cancer 24, 1–21 (2021). https://doi.org/10.1007/s10120-020-01042-y.)

the recommendation that a D2 lymphadenectomy be performed. Current treatment guidelines published by the NCCN, Cancer Care Ontario, and the European Society of Surgical Oncology support the performance of a D2 lymph node dissection and acknowledge that it is preferred over a D1 dissection when it can be safely performed.[4,48,49] Western institutions were slow adopters of the D2 dissection largely because of the initial outcomes of 2 Western trials—the Dutch Gastric Cancer Group Trial and the British Cooperative trial conducted by the Medical Research Council trial—which showed that there was no improvement in overall survival with D2 as compared with D1 lymph node dissection, but there was increased morbidity.[50,51] However, these trials were criticized for including institutions lacking expertise in performing D2 dissection as well as for incorporating routine splenectomy and distal pancreatectomy as part of their procedures, which were thought to have impacted the outcomes. Furthermore, 15-year data from the Dutch trial showed that a D2 lymph node dissection as compared with a D1 dissection was associated with lower local recurrence (12% vs 22%), regional recurrence (13 vs 19%), and gastric cancer–related deaths (37% vs 48%) while still failing to show a difference in overall survival (21% and 29%, $P = .34$).[52] A meta-analysis comparing D1 and D2 lymphadenectomy showed an improvement in disease-specific survival after D2 lymphadenectomy, but there was an increase in postoperative mortality.[53] It should be noted that although D2 is generally recommended as standard for optimal staging and treatment for most patients, in patients with early tumors, advanced age, poor functional status, and multiple comorbidities, D1 or D1+ dissections can be considered on a case-by-case basis.[6] The question of whether to perform a superextended D3 lymphadenectomy has been less controversial, and it is not recommended outside of a select subset of patients, as it has not been shown to have a survival benefit and may increase perioperative morbidity and mortality given its aggressive approach.[53–55]

Although D2 dissection is now supported by major institutions like the NCCN, this does not mean that this recommendation is being followed in the United States. A US randomized trial noted that 54% of patients underwent less than a D1 lymphadenectomy, whereas D1 or $\geq$ procedures were performed in 36% and 10%, respectively.[56] Difficulty in documentation of removal by lymph node stations as well as a desire to unify staging systems with other cancer sites resulted in changes to the N stage of the American Joint Committee on Cancer (AJCC) staging system, which was changed starting with the AJCC fifth edition to follow a numeric system instead of one based on node distance from tumor location. As of the most recent AJCC eighth edition, it required that least 16 lymph nodes be removed and examined at the time of gastrectomy for adequate staging, which is used as a quality metric in the United States in place of documentation of D2 dissection. Studies using number of lymph nodes examined have similarly shown the inadequacy of US lymphadenectomies reporting that less than one-third of US patients had 15 or more lymph nodes removed during their procedures as was the recommendation in the AJCC fifth through seventh editions.[57,58]

Failure to perform an adequate lymphadenectomy may not simply be due to a difference in philosophy, but it may also be that Western surgeons have not been adequately trained how to do this complex procedure and may not be comfortable performing it. The technical demands of performing a D2 lymphadenectomy are well documented, and the literature points to a steep learning curve. Although Western surgeons have reported the feasibility of performing this technique with good outcomes, they have also acknowledged the importance of having these procedures performed in specialized centers by individuals who have been adequately supervised during the steep learning curve.[59,60] In 1 study from Korea, it was reported that the

learning curve for gastric cancer survival did not plateau until after a surgeon had performed 100 operations.[61]

Thus, even though D2 dissection is now supported by Western institutions, training will be required for surgeons to be proficient at this technique. Until that time, these procedures should be performed at selected centers with surgeons with expertise in performing this procedure, which is supported by a meta-analysis that shows the relationship of outcomes after gastric cancer surgery with hospital and surgeon factors.[62] Although there is still significant work that needs to be done in the West to improve rates of D2 dissections, in the future, there may be other advancements in the management of regional lymph nodes that will also have to be adopted. There is growing interest in the use of sentinel lymph node biopsies for patients with early gastric cancer as has been done for other types of cancer; however, this technique has not been refined enough yet, and the data cannot yet support its use.[63–67]

Reconstructive Options

After a partial or total gastrectomy, it is necessary to reconstruct the gastrointestinal (GI) tract. Different procedures have been devised to preserve duodenal continuity, important for preventing loss of fat-soluble vitamins, and jejunal continuity, important for preventing retrograde flow of jejunal contents that can occur when there is disruption in electrical activity initiated by the duodenal pacemaker.[68] Some procedures also include the construction of a gastric pouch to serve as a functional reservoir after gastrectomy. These different reconstructions have been devised to try to limit the effects of postgastrectomy syndromes, but each generally has some degree of early or late dumping because the pylorus is typically removed (see Complications in later discussion).

After a partial gastrectomy, the most common reconstructive procedures are the Billroth and Roux-en-Y reconstructions (**Fig. 4**). The Billroth I reconstruction anastomoses the remnant stomach to the duodenal stump in a primary end-to-end fashion, which in turn preserves duodenal and jejunal continuity. This procedure, which requires a tension-free anastomosis, is not feasible after subtotal gastrectomy or total gastrectomy, which is commonly required for adequate tumor resection. The Billroth II reconstruction anastomoses the remnant stomach to the proximal jejunum in an end-to-side fashion, which preserves jejunal but not duodenal continuity. Gastritis and dumping can be seen after this reconstruction, and it also tends to have some degree of malabsorption of fat-soluble vitamins because of the loss of duodenal continuity. The Roux-en-Y reconstruction anastomoses the remnant stomach to an

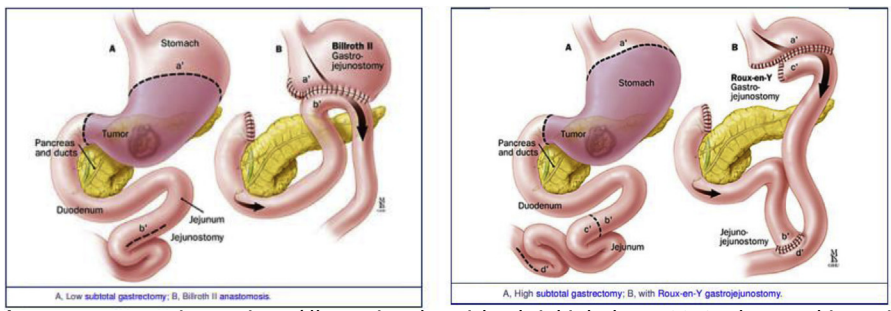


Fig. 4. Reconstruction options. (Illustrations by Michael Linkinhoker © 2013 Johns Hopkins University. All rights reserved.)

isoperistaltic roux limb of jejunum, whereas the proximal jejunum is anastomosed to the distal roux limb in an end-to-side fashion; it is performed to divert the bilious drainage away from the gastric remnant. The Roux-en-Y reconstruction results in less reflux than in the Billroth reconstructions, but it can lead to gastric atony along with the adverse effects of jejunal transection, which contributes to the "Roux syndrome" in which patients develop abdominal pain and vomiting.[6,36] Although the patient's anatomy and surgeon preference often dictate the type of reconstruction that is performed, randomized trials seem to suggest that the Roux-en-Y reconstruction is better tolerated overall and is associated with an improved quality of life compared with the Billroth reconstructions.[69–71]

After a total gastrectomy, GI continuity can be restored with either a Roux-en-Y reconstruction or a bowel interposition technique (jejunal or colon interposition). For a Roux-en-Y approach, a surgeon may elect to perform a straight esophagojejunal anastomosis, a looped esophagojejunal anastomosis, or a jejunal pouch construction, which can be brought behind the colon (Hunt) or in front of the colon (Rodino).[72] The most prevalent reconstruction strategy and the one that is generally recommended is the Roux-en-Y reconstruction.[73,74] Despite some limited data, the literature also seems to favor a jejunal pouch reconstruction, especially in patients who are anticipated to have a longer survival, as it has been associated with better functional outcomes and improved quality of life.[6,75–80]

ADDITIONAL TECHNICAL CONSIDERATIONS

Minimally Invasive Techniques

Like all of surgery, gastric cancer surgery is trending toward the development of more minimally invasive approaches. In addition to endoscopic techniques as described previously, there are also laparoscopic and robotic approaches to gastrectomy, which are gaining in popularity. Like most of gastric surgery, advances are primarily reported in literature from Eastern institutions, but the benefits of these approaches are starting to find their way into the practices and literature of Western institutions. Although an open approach is still widely performed around the world, laparoscopic gastric resection when performed in experienced centers has been associated with a faster recovery with less pain and fewer complications while allowing for comparable lymph node retrieval.[81–84] Laparoscopic gastrectomy is a well-established technique for treating gastric cancer in Eastern countries and, in 2009, accounted for approximately one-quarter of all gastric surgeries performed for cancer in Japan and South Korea.[85] Many Eastern studies have been performed that show the benefit of a laparoscopic technique to early gastric cancer[81,83,86–89] and locally advanced gastric cancer.[82,90–94] A 2016 meta-analysis concluded that laparoscopic gastrectomy resulted in less postoperative morbidity, shorter hospitalization, and higher quality of life with no difference in lymph nodes retrieved, mortality, cancer recurrence, and disease-free survival.[95] Compared with Eastern countries, Western countries have less experience with laparoscopic gastrectomy (performed in approximately 8%–23% of cases[96,97]), but it has also been shown to be beneficial in Western cohorts.[97–99] Although most of the aforementioned studies are in regards to laparoscopic partial gastrectomy, total gastrectomy can also be performed minimally invasively. It is a technically demanding procedure, but when performed by a surgeon with advanced training in a high-volume center, short- and longer-term outcomes are satisfactory.[100–102]

When deciding whether an open or minimally invasive approach should be taken, ultimately the choice depends on several provider and patient factors. Laparoscopic gastrectomy is a technically demanding procedure, especially when a D2

lymphadenectomy and GI reconstruction are also performed, which requires an experienced surgeon who can be supported by staff and hospital resources to assist not only intraoperatively but also in postoperative management. Studies suggest that 40 to 100 cases must be performed for a surgeon to be proficient in this technique.[103–106] Regarding patient factors, the ideal patient is one with early gastric cancer who does not have significant cardiopulmonary comorbidities, obesity, or previous upper abdominal surgery, which may complicate a patient's ability to receive pneumoperitoneum and to have a safe dissection without encountering extensive intra-abdominal adhesions. In addition, many bulky gastric cancers with local invasion into other organs may not be best suited for a laparoscopic procedure. All these factors have to be taken into consideration when deciding what type of surgery should be performed, but the presence of these factors do not necessarily exclude a patient from a minimally invasive approach.

Although Western countries are still catching up to their Eastern colleagues in terms of laparoscopic gastric cancer management, the future of gastric cancer surgery may trend toward robotic surgery, which has been an alternative minimally invasive technique since the early 2000s, yet still remains an emerging technology. In a meta-analysis, robotic surgery was associated with less blood loss, less time to first flatus, and greater lymph node yield than conventional laparoscopic gastrectomy, although this study included no randomized trials.[107] It also found that both approaches had similar postoperative morbidity and mortality. As robotic technology becomes cheaper and more prevalent, it is anticipated that it will take up a larger percentage of the procedures performed for gastric cancer.

Drains and Feeding Tubes

Intraoperatively, some surgeons may elect to place drains and feeding tubes in gastrectomy patients, but in general, the literature does not support this practice, having found no improvement in outcomes and a possible increase in complications with their placement. However, there are some select patients in whom the placement of a small bowel feeding tube can be justified: patients at the highest risk of anastomotic leak and/or malnutrition, such as those undergoing total gastrectomy, and in those patients in whom additional enteral feeding may decrease the time to adjuvant therapy.[6] Although there are no strong recommendations regarding these feeding tubes (the NCCN guidelines only recommend that they may be considered in select patients), their placement still occurs in 24% to 32% of patients.[4,108,109]

Surgical Approach to Metastatic Disease

As new treatments emerge, providers are starting to question the oncologic dogma that metastatic disease should only be treated with systemic therapy. There is some evidence emerging to suggest that in some select patients a more aggressive surgical approach may have some value. In recent years, literature has started to show that a select group of patients with metastatic gastric cancer limited only to the peritoneum without solid organ metastases may achieve a survival benefit by undergoing aggressive cytoreductive surgery and heated intraperitoneal chemotherapy, but further research is needed.[110–113] Furthermore, when it comes to isolated solid organ metastases, such as hepatic and pulmonary, there is some evidence to support the practice of metastasectomy. Hepatic metastasectomy has been reported, but the occurrence of isolated liver metastases is a rare event (only 0.5% in Asian populations). There is currently a lack of consensus as to the appropriate patient selection for this procedure and to whether it should be performed at all given the poor prognosis.[114–116] Similarly,

there are little data to guide the performance of pulmonary metastasectomy, which can potentially result in a benefit for patients, but it is a rare event.

Palliative Interventions

When decision between provider and patient is no longer to pursue cure or life-prolonging treatments, surgery still may have a role in a palliative sense and can include options, such as stenting, palliative gastrectomy, and gastrojejunostomy. Although chemotherapy is the cornerstone of effective treatment for metastatic disease, it often is insufficient to address local symptoms secondary to obstruction, perforation, or bleeding. Patients who present with bleeding may require endoscopy, angiography, or radiotherapy.[117] Patients who present with an obstruction may be managed with endoscopic stent placement, a venting gastrostomy, and in some select patients, a gastrojejunostomy or palliative gastrectomy can be considered.[118] Studies have compared endoscopic stenting with palliative gastrojejunostomy and have found that although there was no difference in efficacy or complications, stenting was associated with shorter hospital stays and faster relief of symptoms, which could be of critical importance to patients with limited remaining time; however, there was a need for more frequent reintervention in those who received stents.[119] Therefore, palliative gastrojejunostomy is generally used in cases where stenting is not deemed to be feasible. It is also considered when longer survival is anticipated. An even more aggressive procedure, a palliative gastrectomy, in general cannot be recommended given its high morbidity, and it is reserved for extremely symptomatic cases where there are no other options. The REGATTA randomized controlled trial examined whether the addition of gastrectomy to chemotherapy improved survival for patients with advanced gastric cancer with a single noncurable factor; however, the study was closed on the basis of futility and found that gastrectomy followed by chemotherapy did not show any survival benefit compared with chemotherapy alone (overall survival at 2 years was 25.1% vs 31.7%, respectively).[120] The decision to pursue any of these interventions must take into account the patient's prognosis and goals in order to limit aggressive therapy at the end of life that is not aligned with the patient's wishes.

POSTOPERATIVE MANAGEMENT, SURVEILLANCE, AND RECURRENT DISEASE

Postoperatively, patients with gastric cancer will be admitted to the surgical floor or a monitored setting based on what is necessary. When possible, enhanced recovery after surgery, and fast-track protocols may be able to be followed,[121,122] particularly for minimally invasive procedures, which emphasize early mobilization and nonnarcotic analgesia. These protocols may improve time to ambulation and oral intake while decreasing length of hospital stay.[123] Although there are no true gold-standard guidelines for postoperative care, patients are started on enteral nutrition as soon as possible, and the involvement of a dietician can be helpful to assist patients in adjusting to their new dietary regimen. Patients are advised to eat small frequent meals high in protein, inclusive of fat, and supplemented by vitamins while avoiding carbohydrates to try to avoid weight loss and nutritional deficiencies.[124] There is some controversy in the literature as to whether routine nasogastric decompression should be performed postoperatively[122,125] and as to whether patients need a postoperative upper GI swallow study.[36]

After patients make it out of the acute postoperative period, they will need to continue to be followed to monitor for recurrent disease. Although NCCN guidelines acknowledge that there are sparse data to guide surveillance strategies, they in general recommend the following: (1) a complete history and physical examination every 3 to 6 months for the first 2 years, every 6 to 12 months for years 3 to 5, and annually thereafter; (2)

complete blood count and chemistry laboratory tests when clinically indicated; (3) Esophagogastroduodenoscopy (EGD) for patients with early-stage disease (TiS or T1a) who underwent endoscopic resection every 6 months for the first year and then annually for either 3 years (Tis) or 5 years (T1a); (4) EGD for patients who underwent surgery as clinically indicated; (5) CT scan with oral and intravenous (IV) contrast based on stage of disease (stage I: as clinically indicated; stage II–III: every 6–12 months for the first 2 years, then annually for up to 5 years).[4] Guidelines from the European Society for Medical Oncology are also somewhat limited in their guidance, suggesting regular posttreatment follow-up with dietary support without providing specifics as to other testing or the frequency of follow-up.[126] When gastric cancer does recur, it can be classified as local or distant recurrence. In general, curative resection is not attempted in patients with locally recurrent disease, although it has been described.[127] Instead, most patients with recurrent disease are offered systemic chemotherapy.

COMPLICATIONS

Despite surgery offering the best chance of cure for patients with gastric cancer, it is not without its risks, and several patients will have complications. Complications can include surgical site infections, intra-abdominal bleeding, anastomotic complications, duodenal/pancreatic/lymphatic fistulas, cardiopulmonary complications, delayed gastric emptying, and postgastrectomy syndromes.[21] The perioperative surgical complications after total gastrectomy are primarily due to anastomotic leak, and long-term complications can include esophageal stricture and the postgastrectomy syndromes. The most worrisome complication in the early postoperative period after total gastrectomy is a breakdown of the esophagojejunal anastomosis, which has been reported to occur in 5% to 7% of patients.[128,129] Although minor leaks without sepsis can be controlled nonoperatively with antibiotics, intestinal decompression, and percutaneous drainage, interventions may be needed for more significant disruptions. Covered stents have been reported to have some success, but major disruptions will need reoperation, and this is associated with increased mortality, which has been reported to be about 30%.[129,130] Anastomotic leak can also result in esophageal stricture, reported in approximately 4% of patients, which usually can be managed with serial endoscopic dilations.[131] The jejunojejunal anastomosis rarely leaks.

Less worrisome but still problematic are the postgastrectomy syndromes.[132,133] Following gastric resection, the motility of the stomach can be affected, resulting in rapid or delayed transit. Rapid transit can be seen with dumping syndrome, which is a phenomenon caused by destruction or bypass of the pyloric sphincter. It can present with symptoms of diarrhea, nausea, vomiting, diaphoresis, sweating, and palpitations. When these symptoms develop early after a meal, it is attributed to the rapid emptying of hyperosmolar chyme into the small bowel; when it occurs late, it is thought to be owing to hypoglycemia that occurs following an insulin peak after eating. Most patients' symptoms will improve with dietary changes.[134] After gastrectomy, some patients may also have delayed gastric emptying, which can be associated with epigastric fullness and emesis. The degree of postsurgical gastroparesis depends on several factors, including whether vagotomy was performed, the extent of stomach and intestinal resection, the extent of lymphatic dissection, and the type of reconstruction performed.[135] Longstanding untreated gastroparesis has significant nutritional and metabolic consequences, which can generally be managed with dietary and behavioral modification in addition to the use of oral prokinetic and antiemetic medications but could potentially require hospitalization in the setting of severe fluid and electrolyte imbalances.[136]

PERIOPERATIVE OUTCOMES

Over the past 2 decades, prognosis for gastric cancer has only improved modestly in the United States, which is indicative of the fact that US gastric cancers are diagnosed at later stages.[137] Regarding perioperative mortality following partial gastric resection, it is low and ranges from 1% to greater than 10% depending on patient age and medical comorbidities.[138–140] For total gastrectomy, perioperative death is reported in trials as ranging from 2% to 13%.[50,141] Regarding longer-term prognosis, it is dependent on patient, tumor, and treatment factors, including histologic type, status of resection margins, age and sex, the stage of disease, its location, the treatment received, and the population studied. In general, Asian populations have been found to have better outcomes than Western populations even when stratified by stage.[142–146] Hypotheses to explain these differences have included differences in treatment (particularly surgical techniques), patient characteristics and behavior, and race-related differences in tumor biology. Although long-term data on quality of life after gastrectomy are limited, studies suggest that these procedures can be performed while maintaining a satisfactory quality of life, which generally improves after the short-term perioperative period.[147–152]

SUMMARY

The management of gastric cancer has evolved over the last several decades and will continue to do so as new therapeutics are developed. At the heart of all gastric cancer treatment has been surgery, and it is likely to stay this way for the time-being. All providers must continue to work together clinically and in research to continue to determine the best types of treatment, their sequence, and timing to achieve the best outcomes for our patients.

CLINICS CARE POINTS

- Staging laparoscopy with peritoneal washings should be performed for gastric cancer clinical stages $\geq$T1b to evaluate for peritoneal spread when chemoradiation or surgery is considered.
- The decision to pursue gastric cancer resection should occur with consultation of a multidisciplinary tumor board to ensure that an appropriate multimodality treatment strategy is planned.
- The goal of gastric resection for adenocarcinoma is to obtain a tumor-free resection margin (R0) on pathologic examination.
- A D2 lymphadenectomy is recognized as the optimal approach to lymph node dissection and should accompany gastric resection when it can be safely performed.
- After gastric resection, Roux-en-Y reconstruction is better tolerated overall and associated with an improved quality of life compared with the Billroth reconstructions.

DISCLOSURE

The authors have no disclosures.

SUPPLEMENTARY DATA

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