REVIEW

SURGICAL RESECTION FOR GASTRIC CANCER: A DESCRIPTIVE REVIEW

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Abstract

In 2012, gastric cancer was the third most common cancer, causing 723,000 deaths worldwide. The purpose of this paper is to explore in detail the surgical resection techniques for gastric malignancies. There is a significant geographic variation in the incidence of this disease around the world, with a predominance in Asia and South America and the lowest numbers are found in North America. For the present review we have searched the relevant articles into the PubMed/Medline and Google Scholar databases. We have used the following keywords: 'gastric' OR 'stomach' AND 'cancer' OR 'adenocarcinoma' OR 'neoplasia' AN D 'surgery' OR 'surgical' OR 'gastrectomy' OR 'lymphadenectomy'. In western countries, with a significant predominance of locally advanced tumors total/subtotal gastrectomy with spleen and pancreas-preserving DII lymphadenectomy by open approach is the standard technique. Laparoscopic radical gastrectomy is the preferred technique, even for locally advanced tumors in Japan, Korea, and China. The surgical approach of patients with gastric cancer is challenging, especially due to increasing use of minimally invasive approach, neoadjuvant therapy, and expanding criteria for resection.

Keywords*: gastric cancer, surgical resection, gastrectomy, lymphadenectomy*

Introduction

In 2012, gastric cancer was the third most common cancer, causing 723,000 deaths worldwide. In the United States, stomach cancer is the 15th most common cancer, and the overall 5-year survival rate was 14.3% in 1975 which rose to 30.4% by 2006-2012 [1]. There is a significant geographic variation in the incidence of this disease around the world, with a predominance in Asia and South America and the lowest numbers are found in North America [2,3]. There is also a predilection of disease in males over females in the United States. In 2015, 16,480 men and 9,890 women were newly diagnosed with gastric cancer [4]. In Western countries, it is still difficult to treat because patients present with advanced stages of the disease. In the United States, the median age at diagnosis is 69 years with less than 2% of cases occurring in persons younger than 35 years. Adenocarcinoma accounts for 90-95% of gastric cancer cases. The other types include lymphomas, gastrointestinal stromal tumors, carcinoids, and squamous cell carcinomas. The management of gastric cancer includes surgical procedures, chemotherapy, neoadjuvant, adjuvant, and palliative therapies. The purpose of this paper is to explore in detail the surgical resection techniques for gastric malignancies.

Materials and method

For the present review, we have searched the relevant articles into the PubMed/Medline and Google Scholar databases. We have used the following keywords: ‘gastric' OR ‘stomach' AND ‘cancer' OR ‘adenocarcinoma' OR ‘neoplasia' AND ‘surgery' OR ‘surgical' OR ‘gastrectomy' OR ‘lymphadenectomy'.

Types of Surgical Approach

There are three main types of tumor resections that exist for the treatment of gastric cancer [5]. The first type is endoscopic resection which is useful during the early stages of the disease. The second type is open surgery, which can be used for subtotal (partial) gastrectomy and total gastrectomy. The third type is laparoscopic surgery. Each type of surgery has its advantages and disadvantages, and each one is used in different types of cases.

Endoscopic surgery is an alternative to surgical resection of mucosal and submucosal neoplastic lesions and intramucosal cancers [6,7]. The Japanese Society for Gastrointestinal Endoscopy (JSGE), has created a classification system based upon visual and endosonographic features for when endoscopic surgery is appropriate for early gastric cancer. To qualify for endoscopic mucosal resection the lesions must meet the following criteria; JSGE type I lesions that are $\leqslant$ 2 cm, JSGE type IIb and IIc lesions that are $\leqslant$ 1cm, and cancers that are limited to the mucosa. For non-ulcerated and larger lesions that involve the submucosa, endoscopic submucosal dissection may be appropriate to employ.

There are two types of endoscopic surgeries employed; endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). The EMR method involves a snare resection of dysplastic lesions while the ESD uses endoscopic tools to dissect lesions from the submucosa. The lesions limited to the mucosa and the superficial layers of the submucosa seem to be the most indicated for the endoscopic cure. It is important to note that both types are used only when the gastric cancer is discovered in its early stages.

Endoscopic mucosal resection was first introduced in 1978. If the circumstances allow, EMR is often the procedure of choice for patients who meet the standard criteria for endoscopic resection of an early gastric cancer. The techniques for EMR are divided into two groups; suction (suck-and-cut) and non-suction (lift-and-cut) techniques. In both techniques that are employed, submucosal injection is commonly used.

The submucosal injection is used to create an undermining submucosal fluid cushion. This cushion that is created may lead to a decrease in the incidence of perforation during the endoscopic mucosal resection. Invasion of the muscularis propria can be suspected if puckering or non-lifting of the lesion occurs. The normal saline solution can be used for the submucosal injection, but it is absorbed quickly. Due to this limitation, other solutions like 50 percent dextrose, hypertonic saline, 10 percent glycerol, 5 percent fructose, sodium hyaluronate, hydroxypropyl methylcellulose (HPMC), and sodium hyaluronate have all been used. The preferred solution for this procedure is HPMC due to its financial advantage and because it is widely available. Between 10 to 40 ml of solution should be injected to achieve an effective submucosal fluid cushion. An injection needle is used at one or multiple sites adjacent to the lesion to attempt to lift the lesion away from the muscularis propria.

In the suction technique, the lesion is lifted away from the muscularis propria by the submucosal fluid cushion and then it is aspirated and resected. The technique is widely performed by using a transparent cap that is affixed to the tip of the endoscope (also known as cap-assisted EMR, EMRC). The cap is placed on top of the lesion and suction is applied to draw the lesion into the cap. The lesion is resected using a snare that is placed through the endoscope into the cap. It is suggested to inject between 20-40 ml of saline to raise the lesion with controlled suction and snaring at the middle of the submucosal fluid cushion rather than the base, to minimize the risk of perforation.

A variation of the suction technique is the band and snare procedure. In most cases, this procedure does not require submucosal injection. In this technique, the tissue is banded using an esophageal variceal banding device and then is snared off in the standard fashion. For this procedure, a large channel endoscope is recommended because it facilitates generation of adequate suction before resection.

The non-suction technique uses a grasping device to pull the lesion away from the muscularis propria, and then a snare is used to resect the lesion. The non-suction techniques were used first and are technically more challenging than the suction methods. The non-suction methods include endoscopic double-snare polypectomy, strip biopsy (using a partial hood), strip biopsy (lift-and-cut), strip biopsy (cutting method), endoscopic resection with local sodium hyaluronate injection, and endoscopic resection with local saline epinephrine injection.

Endoscopic submucosal dissection has been used to treat gastric subepithelial tumors, like gastrointestinal stromal tumors and leiomyomas. ESD is an alternative to EMR in which a specialized needle-knife is used to dissect lesions from the submucosa. ESD allows the possibility to remove mucosal and submucosal tumors en bloc. It is most useful for the treatment of early gastric cancer but has also been applied to lesions in the esophagus, the esophagogastric junction, the duodenum, and the colon.

Subtotal and total gastrectomy is carried out by open surgery which entails making a large incision in the skin of the abdomen to remove the stomach. An alternative to this procedure is laparoscopic surgery, which allows the surgeon to remove the stomach through several small incisions made in the abdomen. Open gastrectomy remains the favored type of surgical treatment for gastric cancer throughout the world. In centers that have more experience, laparoscopic gastric resection can be performed, which offers patients fewer complications and a quicker recovery time.

Laparoscopic gastrectomy is mainly performed in cases of early gastric cancers. Early gastric cancer is defined as invasive gastric cancer that does not invade deeper than the submucosa. Although the operative time for laparoscopic procedures is generally longer than that for conventional open gastrectomy, laparoscopic gastrectomy is superior to open surgery by virtue of its reduced surgical invasiveness, less postoperative pain, earlier hospital discharge, lower hospital cost, better cosmesis, and a better quality of life as a result of smaller skin incisions and minimized trauma to the abdominal wall [8].

There are three types of laparoscopic surgeries for the treatment of early gastric cancer; laparoscopic wedge resection (LWR), intragastric mucosal resection (IGMR), and laparoscopic gastrectomy (totally laparoscopic, laparoscopy-assisted, and hand-assisted) [9]. LWR or IGMR can be used to treat early gastric carcinoma that does not have risk factors for lymph node metastasis. Conversely, a laparoscopic gastrectomy, like laparoscopy-assisted distal gastrectomy (LADG), was developed to treat early gastric carcinoma if there is a potential risk of lymph node metastasis at the perigastric portion (N1). The Guidelines for Gastric Cancer Treatment of the Japanese Cancer Association consist of two indications for LADG: (1) mucosal carcinoma without preoperatively diagnosed lymph node metastasis, and (2) carcinoma with submucosal invasion and without preoperatively diagnosed lymph node metastasis. At times, it is difficult to diagnose preoperatively a lymph node metastasis, therefore the indications for LWR, IGMR, and LADG are determined by the histological type, tumor size, depth of cancer invasion, and the presence of ulceration.

Laparoscopic surgery for gastric cancer is potentially better than a traditional laparotomy regarding short-term benefits. The technique is deemed safe and can fulfill the oncological criteria for surgery. Several studies have concluded that laparoscopic surgery reduced intraoperative blood loss, postoperative pain, length of hospital stay, and postoperative morbidities while recovering a similar number of lymph nodes compared with open surgery [10,11]. In the largest randomized trial, which included 1416 patients with early gastric cancer, laparoscopic distal gastrectomy resulted in a

lower wound (3.1 versus 7.7 percent), intraabdominal (7.6 versus 10.3 percent), and overall (13 versus 20 percent) complication rates compared with open distal gastrectomy [12]. Although the studies demonstrate the short-term advantages, longer-term data from randomized trials should be carried out to consider laparoscopic surgery oncologically equivalent to open surgery for the treatment of invasive gastric cancer.

Types of Gastric Resections

Currently, the only curative treatment for gastric carcinoma is surgical resection [13]. There are a number of procedures that can be performed which depend on the degree of local extension and localization of the tumor [14]. The most radical surgery that exists is a total gastrectomy. In the case of localized tumors, a partial gastrectomy can be performed. Some form of subtotal gastrectomy is the most employed surgical procedure. A total gastrectomy, if required, involves the removal of the whole stomach, the greater omentum, usually removal of the spleen and sometimes includes the lower portion of the esophagus if the tumor is located proximally. In a radical subtotal gastrectomy, 80% of the stomach is removed with the omentum as well as part of the duodenum.

A subtotal gastrectomy with a DII lymph-node dissection can be performed through either a bilateral subcostal or an upper midline incision. A Goligher retractor is then placed for exposure. The abdomen is fully explored to assess the resectability of the primary tumor and to find any other areas of occult metastatic disease. The left lateral segment of the liver is then mobilized by incision of the left triangular ligament and folding the lobe underneath itself with light pressure from a self-retaining retractor.

Following the previous maneuver, the stomach is exposed, and the lesser sac is entered by dissecting the greater omentum from the transverse colon. The peritoneum that overlies the cephalic portion of the transverse mesocolon is dissected upwards with caution to not mistakenly injure the middle colic vessels. In some patients, this dissection is not possible due to the fusion of the peritoneum to the mesocolon. In case of a non-fused peritoneum, the dissection is continued beyond the base of the mesocolon to the inferior edge of the pancreas. The peritoneum and fatty tissue that lie over the pancreas are dissected cephalically. Once the lesser sac is entered, the dissection proceeds following an avascular plane, whilst moving to the patient's right until the right gastroepiploic vessels are identified and ligated. To achieve an adequate mobilization of the duodenum and pylorus, the Kocher maneuver should be performed. The operating surgeon continues clockwise, with dissection of the hepatoduodenal ligament. The right gastric vessels are then identified and ligated. Lymphadenectomy of the suprapyloric and hepatoduodenal lymph nodes is performed.

Next, the first portion of the duodenum and pylorus are mobilized adequately to achieve a margin that is free of any tumors and to safely close the duodenum. The duodenum is transected with a stapling device about 2 cm distal to the pylorus. The staple line is then over sewn with a row of interrupted 3-0 silk Lambert sutures. The lesser omentum is moved inferiorly from its attachments to the liver along with the lymph-node tissue which also lies inferior to the hepatic artery. An anatomical variant may be present with an aberrant or accessory left hepatic artery that may originate from the left gastric artery and resides in the lesser omentum. The aberrant artery that may be present should be preserved in conjunction with the main left gastric artery.

To expose the left gastric artery, the stomach and omentum are retracted cephalically, and it is then doubly ligated at its origin and divided. The DII lymph nodes that surround the celiac axis are dissected along the aorta from the celiac trunk to the superior border of the pancreas to the left along the splenic vessels. The proximal line to transversely dissect the stomach is approximately 5 cm from the tumor. The greater and lesser omentum are dissected from the stomach at the proximal transection site. The proximal stomach is then transversely dissected using a 90-mm stapling device. After the

histologic investigation and analysis are performed and there is confirmation that there are disease-free resection margins, the reconstruction procedure can be performed.

A total gastrectomy can be performed by simply extending the area of the proximal dissection of the subtotal gastrectomy, as previously described. After the dissection of the duodenal region and DII lymphadenectomy are complete, and the omentum is mobilized away from the transverse colon, the dissection is continued along the greater curvature by dividing the gastrosplenic ligament and each of the short gastric vessels. A very careful dissection is required during this part of the procedure to avoid excessive traction, which could result in a capsular tear of the spleen.

Next, the dissection along the omentum is continued and extended up to the esophagus. The left lateral lobe of the liver is retracted medially so that the esophagus can be identified by palpation of the nasogastric tube, and then the peritoneum is divided along its intra-abdominal portion. A Penrose drain is placed around the esophagus to assist in the dissection. The following step in the procedure is to identify the vagus nerves and to divide them above the esophagogastric junction.

After the esophagus is divided, a frozen-section pathologic evaluation is performed due to the frequency of unsuspected proximal lymphatic infiltration of the tumor. Once the specimen is removed and a disease-free margin is confirmed histologically, a Roux-en-Y, end-to-side esophagojejunostomy is executed. On the lateral aspects of the esophagus, stay sutures are placed. The Roux limb is then raised up either antecolic or retrocolic. A point, approximately 8-10 cm from the end of the Roux limb is used for the end-to-side anastomosis. A circular stapling device or a two-layer hand-sewn anastomosis is performed. Regarding the stapled anastomosis, the staple line at the end of the Roux limb is removed. The appropriate-sized circular stapler is then slipped through the Roux limb. A 2-0 Prolene purse-string suture is then placed at the end of the esophagus, and the anvil of the circular stapler is introduced into the esophagus. The purse-string suture is then fastened and the stapler is engaged. Once the stapler is removed, the end of the jejunal limb is closed using a linear stapler. Finally, a nasogastric tube is placed down the efferent limb.

In some cases where the large gastric tumor has reached adjacent organs, an extended gastrectomy must be performed. Large gastric tumors that run along the posterior wall of the antrum or body of the stomach may also extend into the pancreas or retroperitoneal structures. In these cases, the spleen and distal pancreas should be removed together with the stomach.

The procedure begins by mobilizing the splenic flexure in order to gain better exposure of the spleen. The colonic and retroperitoneal attachments to the spleen are then divided. The distal pancreas and spleen are elevated and brought to the midline. The splenic artery and vein are transected, and the pancreas is then divided at the level of the mesenteric vessels. The remaining pancreas must be ligated at the pancreatic duct using a 5-0 Prolene suture and closure of the pancreatic stump with 3-0 Prolene mattress sutures. Next, a closed suction drain is placed near the pancreatic closure.

In some cases, the gastric carcinoma can locally invade the left lateral lobe of the liver. This means a direct invasion of the tumor has occurred, not metastatic disease. If inflow occlusion is necessary, an umbilical tape is placed around the porta hepatis. For hemostatic control along the liver transection line, an overlapping large 0 chromic liver suture is applied. Using an electrocautery unit or an ultrasonic dissector, the liver tissue is then divided with at least a 1-cm gross margin. The rest of the gastrectomy is performed in the standard fashion. Any large tumors that arise along the greater curvature of the stomach can invade either the transverse colon itself or the transverse colon mesentery. This situation may require resection of the stomach together with the transverse colon. A primary colon resection is performed with re-anastomosis of the colon, after proper antibiotic and mechanical bowel preparation is completed.

Types of Lymphadenectomy

Lymphadenectomy can also be performed but is the subject of intense debate. It is based on the principle that a radical resection, including extensive removal of lymph node tissue, could result in improved outcomes. In

Japan, gastric cancer occurs more frequently than in Western countries. This has led Japan to create a standardized radical lymph node dissection. Japanese surgeons routinely perform extended lymphadenectomy, which has shown to have a therapeutic benefit and some improved long-term survival rates compared to Western countries.

The Japanese surgeons have meticulously divided the draining lymph node basins of the stomach into 16 stations [15]. These lymph-node stations are classified into three groups that correspond to the location of the primary tumor and reflect the likelihood of harboring lymph-node metastases [16]. The 1st to the 6th stations are perigastric, and the remaining ten are located around the great vessels, behind the pancreas, and along the aorta. The first group (#1-6) is the perigastric lymph nodes. The second group includes the lymph nodes at the base of the left gastric artery (#7), along the common hepatic (#8), along the celiac axis (#9), splenic (#11), and proper hepatic arteries (#12). The periaortic lymph nodes (#16) comprise the third group.

The most comprehensive and worldwide accepted lymph node dissection for gastric cancer is the Japanese Classification of Gastric Cancer. According to the extent of dissected areas, can be described: (a) the DI lymphadenectomy, which includes the perigastric lymph nodes (station 1 to 6); (b) the DII lymphadenectomy, which involve additional removal of lymphatic tissue along the hepatic, celiac, left gastric, and splenic arteries (stations 1 to 12); (c) the DIII dissection, which comes with no additional oncological benefits over DII, includes periaortic nodal dissection (station 1 to 16).

To resolve the debate, various authors and researchers have brought forward different ideas regarding the positive and negative aspects of gastric cancer with lymphadenectomy. The argument supporting extended lymphadenectomy is that by removing a larger number of lymph nodes one can more accurately stage the disease and to not remove them leaves behind the diseased tissue, which can be potentially fatal. If the staging is more accurate, then one can minimize migration. The better results in Asian patients may be related to the resulting improvement in stage-specific survival.

There are two main arguments against the systematic use of an extended lymphadenectomy. The first is that there is an associated increase in morbidity and mortality, particularly when splenectomy is performed with the extended lymphadenectomy. The second is the apparent lack of survival benefit for extended lymphadenectomy that is evidenced in most large randomized trials.

Multiple prospective randomized trials in Asian and Western populations have failed to show an overall survival benefit with DII versus DI lymphadenectomy [17,18]. The same applies for DII versus DIII lymphadenectomy. Two of the three separate meta-analyses comparing DI versus DII node dissection have concluded that there is no survival benefit to DII lymphadenectomy, although the most recent and inclusive analysis of five randomized controlled trials did find a modest advantage for DII lymphadenectomy in terms of disease-specific survival, which was counterbalanced by a twofold higher rate of postoperative mortality [17,19]. Both of the meta-analysis studying the benefit of DII versus more extended lymphadenectomy have concluded that there is no significant survival benefit from extended lymphadenectomy [20].

As mentioned previously, the majority of the randomized trials have failed to demonstrate a survival benefit for DI versus DII nodal dissection in patients with invasive gastric cancer. However, it is important to note, many clinicians consider that the two largest trials (the Dutch and the Medical Research Council [MRC] trials) were flawed and under-powered to show survival advantage to DII lymphadenectomy. In summary, based upon the most recent analysis of the Dutch trial and the 2015 Cochrane analysis, DII dissection is preferred in patients with potentially curable gastric cancer.

The DII versus DIII lymphadenectomy is also widely studied to provide the best patient outcomes. The 2015 Cochrane analysis of the Japan Clinical Oncology Group (JCOG) trial and two other smaller randomized trials of DII

versus DIII (with PAND) dissection, concluded that resection of the para-aortic nodes did not provide any significant survival benefit [20]. Moreover, while there was no significant difference in perioperative mortality with extended lymphadenectomy, the 95 percent confidence intervals were very wide (RR 1.67, 95% Cl 0.41-6.73) and included the possibility of almost a sevenfold increased risk of perioperative mortality. Following this information, para-aortic lymphadenectomy should not be implemented as a routine practice for surgical treatment of gastric cancer.

Despite much debate regarding lymphadenectomy with gastric cancer, some conclusions can be drawn. Most major cancer centers are performing a DII compared to a DI dissection due to the apparent impact of DII lymphadenectomy on disease-specific survival. A DII lymph node dissection is preferred over a DI dissection, as recommended by the published treatment guidelines of the National Comprehensive Cancer Network (NCCN). Although this is the recommended procedure, the related increased reported rates of operative mortality should be taken into consideration and should be tempered by where and by whom the operation is being performed.

There is no room for increased operative mortality when a survival benefit of extended lymphadenectomy is to be gained. A spleen and pancreas preserving DII lymphadenectomy provides superior staging information and can provide a survival benefit, simultaneously avoiding excess morbidity. A splenectomy that is performed during gastric resection for tumors that are not adjacent to or invading the spleen or the tail of the pancreas increases the morbidity and mortality rates without improving survival. Therefore, splenectomy is recommended only in cases where there is a direct tumor extension.

Conclusions

Surgical approach of patients with gastric cancer is challenging, especially due to an increasing use of a minimally invasive approach, neoadjuvant therapy, and expanding criteria for resection.

Author contributions

Christina Lee Tache wrote the first draft of the manuscript, Ionut Negoi Mircea Beuran reviewed the manuscript; all authors approved the final version of the manuscript.

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