

Totally Laparoscopic Gastrectomy for Gastric Cancer

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ABSTRACT

Background and Objectives: Recent studies have supported minimally invasive techniques as a viable alternative to open surgery in the treatment of gastric cancer. The goal of this study is to review our institution's experience with totally laparoscopic gastrectomy for the treatment of both early- and advanced-stage gastric cancer.

Methods: A retrospective study was conducted to examine the short-term outcomes of laparoscopic gastrectomy performed at Monmouth Medical Center between May 2003 and June 2012. We reviewed postoperative complications, surgical margins, number of resected lymph nodes, estimated blood loss, length of stay, narcotic use, and recurrence rate.

Results: Forty patients were included in the study. There were 21 cases of adenocarcinoma, 15 cases of gastrointestinal stromal tumor, 2 cases of carcinoid, 1 case of small cell neuroendocrine tumor, and 1 case of squamous cell carcinoma. The mean operative time was 220 minutes (range, 67–450 minutes). The median length of stay was 6 days (range, 1–37 days). The mean number of harvested lymph nodes was 11. Early postoperative complications occurred in 7 patients and included anastomotic stricture, wound infection, intra-abdominal abscess, bowel obstruction, and esophageal pneumatosis. There were two deaths. The Kaplan-Meier 5-year overall and recurrence-free survival rate for all cases of adenocarcinoma was 63.2%.

Conclusions: Totally laparoscopic gastrectomy is a reasonable option for the treatment of gastric malignancy, with early data showing acceptable survival rates and perioperative outcomes. Large-scale randomized trials are

still needed to confirm oncologic equivalency to open gastrectomy in patients with advanced disease.

Key Words: Gastric cancer, Laparoscopic gastrectomy.

INTRODUCTION

The role of laparoscopy in gastric cancer (GC) therapy is evolving in the United States. As American surgeons develop more advanced laparoscopic skills, we need to establish the circumstances in which laparoscopy is most effective for the treatment of GC. Previous studies have shown that laparoscopic gastrectomy (LG) has operative and postoperative benefits for patients.^{1–3} In addition, preliminary data suggest that LG may have similar morbidity and mortality rates as well as comparable oncologic outcomes with the traditional open approach to the treatment of GC.^{4,5} Although the advantages of laparoscopy are evident, surgeons need to establish proper indications, effective technique, and acceptable results for laparoscopy in GC surgery.

Surgeons in Japan have pioneered the use of laparoscopy in the treatment of GC because of its increased incidence and resectability in the East compared with Western countries.^{6–8} By comparison, American surgeons have less experience in treating GC laparoscopically. This inexperience and the complexities of LG may contribute to a lack of data from US institutions pertaining to this modality in the treatment of GC.

The predicted limitations of laparoscopy in GC surgery are related to the technical aspects of the operations, as well as the possibility of inadequate treatment in an oncologic setting.⁹ Comparisons have been made to the advancing surgical therapies in other types of cancer. In the treatment of colon cancer, laparoscopic colon resections were not inferior to an open approach in direct measures of survival and recurrence.¹⁰ Laparoscopic colon resection also resulted in a lower risk of adverse events, blood transfusion, and wound infections.¹¹ Concerns have been raised regarding potentially increased rates of tumor dissemination and recurrence because of differences in tumor biology and recurrence patterns of GC.¹² This may

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suggest that data from laparoscopic resection of other types of cancer are not necessarily applicable to this disease.¹³ However, encouraging data have emerged from Japanese studies showing the effectiveness of a laparoscopic-assisted approach in early-stage GC in terms of recurrence and survival rates.⁵ Similar smaller studies have been performed in the United States with survival data indicating that laparoscopy is comparable with open surgery.^{1,13}

Most of the existing data from previous studies on LG for GC have concentrated on a laparoscopically assisted (LA) approach. Mochiki et al¹⁴ describe an LA technique in which most of the dissection was performed laparoscopically and the esophagogastric anastomosis was performed through a midline laparotomy incision. The operative time, number of lymph nodes, complication rate, and 5-year cumulative and disease-free survival rates in this study were similar to those with an open approach. A clinical trial by Lee et al¹⁵ described an LA approach to distal gastrectomy and a D2 lymph node dissection that resulted in no deaths and a 3% complication rate in a series of 64 patients. Although LA gastrectomy is a useful approach, a totally laparoscopic approach to GC may provide added benefit.

Totally laparoscopic gastrectomy (TLG) uses smaller incisions and may maximize the postoperative benefits of laparoscopy. When compared with open surgery for GC, TLG resulted in similar morbidity and mortality rates, as well as faster recovery of gastrointestinal function, a reduction in blood loss, and shorter hospital stays.¹⁶ One study reported a significant improvement in postoperative pain scores and a decreased need for analgesics among those patients who underwent a TLG for GC.¹⁷

In addition to operative results, oncologic outcomes resulting from the totally laparoscopic treatment of GC must be carefully evaluated. A retrospective review of a totally laparoscopic approach to subtotal and total R0 gastrectomy for all stages of GC reported overall and disease-free 5-year survival rates of 59% and 57%, respectively.¹⁸ A matched-cohort study comparing TLG with open gastrectomy for GC reported comparable overall and stage-by-stage 3-year survival.³ These data would suggest acceptable oncologic outcomes for TLG compared with the open approach.

We assessed our own institution's experience using a totally laparoscopic approach for the treatment of both early- and advanced-stage GC by describing our operative technique and analyzing operative, early postoperative, and long-term data.

PATIENTS AND METHODS

The first laparoscopic gastric wedge resection at Monmouth Medical Center was performed in 2003 for a small gastrointestinal stromal tumor (GIST). Later that year, our surgeons began performing subtotal resections with a Billroth II anastomosis for middle and distal-third gastric tumors and performing total gastrectomy with Roux-en-Y reconstruction for proximal-third tumors. GISTs were excised by laparoscopic wedge resection when possible. All cases of early-stage adenocarcinoma underwent D1 lymphadenectomy, with D2 lymphadenectomy reserved for patients with preoperatively diagnosed advanced-stage disease or with bulky lymphadenopathy noted intraoperatively (in incidental or emergent cases in which preoperative staging might not have been possible). Patients with a preoperatively diagnosed hiatal hernia were treated with concurrent hernia repair and posterior crural closure.

Preoperative workup for all cases of adenocarcinoma and GIST included upper endoscopy with biopsy in all but 3 cases that were discovered incidentally. In cases of adenocarcinoma, computed tomography and endoscopic ultrasonography were used to further evaluate tumor invasion and metastases in 86% and 43% of cases, respectively. Endoscopic ultrasonography was not performed consistently in all cases of adenocarcinoma before its recommendation as a preoperative staging tool by the National Comprehensive Cancer Network.¹⁹ Computed tomography and endoscopic ultrasonography were used to further evaluate select cases of GIST 47% and 53% of the time, respectively, according to current National Comprehensive Cancer Network guidelines.²⁰

Patient Characteristics and Selection

Between May 2003 and June 2012, 51 patients underwent LG for a preoperative diagnosis of GC. Of these patients, 7 were excluded on the basis of the final pathology results, which showed no carcinoma. These excluded cases involved lipomas (2), high-grade dysplasia (1), ulcer (1), pancreatic heterotopia (1), inflammatory myofibroblastic tumor (1), and hyperplastic polyp (1).

Four patients were unable to be treated with a curative resection because of metastatic or unresectable disease at the time of surgery and instead underwent a laparoscopic palliative procedure. These included 3 gastrojejunostomies and 1 jejunostomy tube. The 40 remaining patients included in this study underwent a totally laparoscopic gastric resection for gastric carcinoma with curative intent.

This study did not use a randomized selection process. The feasibility of a laparoscopic approach was considered in all cases of GC, regardless of stage, diagnosis, or patient body habitus. All cases were therefore initially attempted laparoscopically per the preference of the operating surgeon and converted to open as indicated. Final decisions regarding surgical approach were made by the attending surgeon and determined by tumor type, size, and location.

Operative Technique

Subtotal gastrectomy. The patient was placed in a supine lithotomy position. General endotracheal anesthesia was used for all procedures, and preoperative antibiotics were given. All patients received a Foley catheter and a nasogastric tube. A Veress needle was inserted at the left subcostal midclavicular line, and pneumoperitoneum was obtained by insufflating the peritoneal cavity with carbon dioxide to a pressure equal to 15 mm Hg. A left paramedian optical port was inserted under direct visualization. A 30° laparoscope was used in all cases. Additional ports were placed as follows: a left subcostal 12-mm port, a left mid-axillary 5-mm port, and 2 right subcostal 5-mm ports. A liver retractor was used to lift the left lobe of the liver. If a hiatal hernia was noted, it was reduced and diaphragmatic reconstruction was performed at this time. Mobilization of the duodenum was performed approximately 1 cm distal to the pylorus. The duodenum was then transected with an Endo-GIA 3.5–60 cartridge (Covidien, Mansfield, MA, USA). Upper endoscopy was used to locate the position of the tumor and evaluate for adequate margins as well as the integrity of the staple line. The stomach was then completely mobilized by taking down the gastrocolic and gastrosplenic ligaments. The short gastric vessels were also divided. The pars flaccida was incised over the caudate lobe, and the right crus of the diaphragm was exposed. At this point, the stomach was divided transversely above the incisura angularis. The right gastric artery was then clipped and transected. The remainder of the stomach was then completely mobilized, and the specimen was placed in an EndoCatch bag (Covidien, Mansfield, MA, USA) and left within the peritoneal cavity until the end of the operation. At this point, the transverse mesocolon was elevated and the ligament of Treitz identified. The bowel was run for approximately 45 cm, and the jejunal loop was brought up to the proximal stomach for creation of the gastrojejunostomy by use of a linear stapler. The anastomosis was then tested by insufflation of both air and methylene blue. After afferent and efferent limb patency was ensured, the liver retractor was removed from the abdomen, and the specimen was removed

through a 2-cm extraction site located just above the umbilicus to the right of the midline. The fascial defect was closed with a figure-of-8 No. 1 polydioxanone stitch. A Jackson-Pratt drain was placed in the left subdiaphragmatic region after all procedures.

Total gastrectomy. Patient placement, trocar setup, and initial mobilization for total gastrectomy were similar to those for subtotal gastrectomy. The gastrocolic and gastrosplenic ligaments were then divided, and the retrogastric pancreatic folds were taken off of the posterior wall of the stomach. The left gastric artery and vein were identified and divided with a linear vascular stapler, obtaining a high ligation just above the takeoff of the celiac axis. Dissection around the crura was performed by incising the peritoneal reflection adjacent to the right crus and continuing toward the left side. A Penrose drain was placed for retraction, and posterior mediastinal dissection was then performed by entering the chest and circumferentially mobilizing the esophagus. The distal esophagus was divided by firing a 3.5-mm linear stapler, and the specimen was placed in a large EndoCatch retrieval bag. At this point, a Roux-en-Y reconstruction was performed. The ligament of Treitz was first identified, and the small bowel was run to approximately 45 cm and divided with a 2.5-mm linear stapler. Two additional 45 mm cartridges with 2.0 mm staples were used for mesenteric transection to obtain enough length to position the Roux limb at the level of the diaphragm with no tension. An enteroenterostomy was created and the mesenteric defect closed with a running nonabsorbable suture. The Roux limb was brought to the esophageal pouch, and the 25-mm anvil was advanced by anesthesia through the mouth into the pouch. With an ultrasonic dissector, the staple line was opened to the mid portion of the esophageal pouch to allow passage of the tip of the nasogastric tube. The nasogastric tube was then pulled until the anvil was secured in the pouch. The doughnuts were inspected to verify that they were intact. The remaining opening was closed with an Endo-GIA 60 mm stapler with 3.5 mm staples.

Postoperative Management

Nasogastric tubes and Jackson-Pratt drains were used routinely. An upper gastrointestinal series was performed on postoperative day 1. If the study was normal, the nasogastric tube was removed and a clear liquid diet was started. The diet was advanced as bowel function returned, and use of Jackson-Pratt drains was discontinued before discharge. Patients were discharged once able to tolerate a

regular diet. Initial follow-up visits were at 1 and 4 weeks in the surgeon's office, with oncology as indicated.

Statistical Analysis

The SPSS software package (version 18.0 for Windows; SPSS, Chicago, IL, USA) was used to perform the statistical analysis. Recurrence-free and overall survival probabilities for cases of adenocarcinoma were estimated with the Kaplan-Meier method.

RESULTS

Patient Demographic Characteristics

There were 40 patients included in this study who underwent curative LG for GC between May 2003 and June 2012. Among these, there were 23 women and 17 men with a mean age of 68 years (range, 48–90 years). Procedures consisted of 26 subtotal gastrectomies or partial gastrectomies (65%), 9 total gastrectomies (23%), and 5 esophagogastrectomies (13%), with an 8% overall conversion rate. Early-stage disease (T1), as defined by the International Union Against Cancer/American Joint Committee on Cancer (AJCC) staging guidelines, was found in 7 patients (33%) with adenocarcinoma.²¹ Of the 21 patients with adenocarcinoma, there were 9 stage Ia/Ib tumors (43%), 3 stage II tumors (14%), and 9 stage III tumors (43%) (Table 1).

Perioperative Outcomes

Three cases necessitated conversion to open surgery because of extensive tumor involvement in the adjacent structures, patient instability due to preoperative perforation, and equipment malfunction.

The mean operative time for all cases was 220 minutes (range, 67–450 minutes), and 35% of cases included an additional procedure. Additional procedures included hiatal hernia repairs (9), splenectomy (2), partial pancreatectomy (1), salpingo-oophorectomy (1), excision of gastrocutaneous fistula (1), cholecystectomy (1), laparoscopic banding (1), and low anterior resection (1) (for concurrent colon cancer). The mean blood loss was 103 mL (range, 5–750 mL). The median number of days of intravenous narcotic use was 3 days (range, 1–12 days). The median length of stay was 6 days (range, 1–37 days). Four cases had prolonged admissions (≥ 3 weeks), and these involved patients with advanced disease and multiple comorbid conditions. Of these, one tumor was discovered incidentally during another procedure and one case was performed emergently for bleeding.

There were no intraoperative complications. Postoperative complications (≤ 30 days) occurred in 7 patients. These included two deaths, one in a patient who underwent gastrectomy after a failed endoscopic mucosal resection and the other after a case performed emergently for bleeding. Esophageal pneumatosis developed in one patient, who was later transferred to hospice care (6 weeks after surgery). This case involved an emergent operation because of perforation from advanced disease. Complications also included wound infection (1), intra-abdominal abscess (1), anastomotic stricture (2), and bowel obstruction requiring reoperation (1). Overall, the postoperative morbidity and mortality rates were 13% and 5%, respectively.

Pathology

Most tumors (53%) were adenocarcinoma on final pathologic analysis. Thirty-eight percent were GIST, 5% were

Table 1.
Patient Demographic Characteristics for All Patients Undergoing Laparoscopic Gastrectomy With Curative Intent

	Adenocarcinoma	GIST	Carcinoid	Other	Total
Total cases	21 (53%)	15 (38%)	2 (5%)	2 (5%)	40
Female gender	12 (57%)	10 (67%)	0	1 (33%)	23 (58%)
Mean age (y)	71	65	63	69	68
Prior EMR ^a /staging laparoscopy	4 (19%)	0	0	0	4 (10%)
Stage Ia/Ib	9 (43%)	11 (73%)	0	1 (50%)	21 (53%)
Stage II	3 (14%)	3 (20%)	1 (50%)	0	7 (18%)
Stage III	9 (43%)	1 (7%)	1 (50%)	1 (50%)	12 (30%)

^a EMR = endoscopic mucosal resection.

carcinoid, and 5% were other pathology (squamous cell carcinoma and small cell neuroendocrine carcinoma). There were 5 cases with positive resection margins; 1 of these involved a large GIST discovered incidentally. Of the 4 cases of adenocarcinoma with positive margins, all were stage III disease; 3 involved cases of linitis plastica, 1 was incidentally discovered, and 1 case was emergent. Two cases underwent subtotal gastrectomies (one converted to open after stapler malfunction), 2 underwent total gastrectomies, and 1 underwent a wedge gastrectomy (GIST). Of the 5 patients with positive margins, 3 died of disease-related causes. A mean of 11 lymph nodes (range, 2–24) were removed, and 14 patients (67%) with adenocarcinoma had lymph node involvement at the time of the original procedure. According to the AJCC guidelines, 22% of stage I and 56% of stage III cases had an adequate lymph node resection (**Figure 1**).²¹ Fifty percent of total gastrectomy and esophagogastrectomy cases underwent adequate lymph node harvest (**Figure 2**).²¹

The mean follow-up for all patients was 39 months (range, 1–114 months). Local recurrence developed in one patient (3%) 6 years postoperatively, and she underwent conversion of a Billroth II anastomosis to a total gastrectomy with Roux-en-Y reconstruction. She originally presented with stage III disease and had adequate lymph node retrieval with a positive margin. Although this was the only known case of recurrence, 6 of the 8 deaths in this series appeared to be cancer related based on data reviewed by our institution’s tumor registry. All disease-related deaths occurred within 1 year after surgery. There were no cases

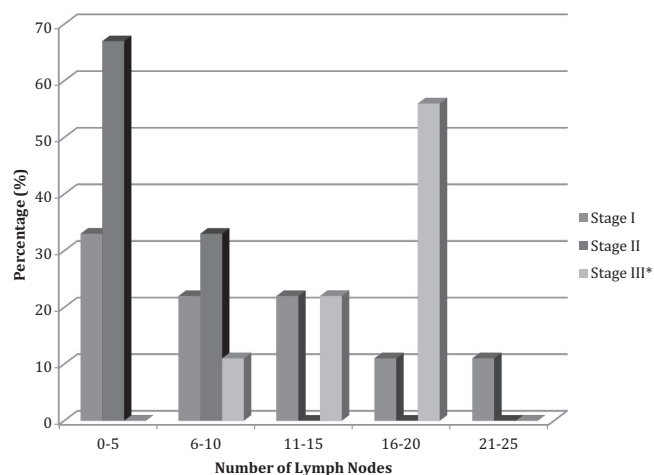


Figure 1. Lymph node harvest by tumor stage, showing the percentage of each tumor stage for which a given number of lymph nodes were retrieved. One patient with stage III disease was excluded because of a lack of lymph node data (asterisk).

of recurrence within the first 5 years of the study period. As such, the overall 5-year survival and disease-free survival rates were equivalent, at 63.2% (95% confidence interval, 38.8%–87.6%), as calculated with the Kaplan-Meier method (**Figure 3**).

DISCUSSION

Laparoscopy has become a common approach to abdominal surgery; however, the treatment of intra-abdominal malignancy by laparoscopy remains a topic of controversy. There are concerns regarding the achievement of an equivalent oncologic resection when compared with an open approach. In addition, the learning curve associated with these technically challenging procedures has slowed the advancement of minimally invasive techniques, particularly in the treatment of GC.²²

Western countries have been slow to adopt the laparoscopic approach for the treatment of GC because surgeons in these countries have less experience treating the disease than in the East.⁷ As a result, Western screening guidelines are much less stringent than in places such as Eastern Asia, where the incidence of GC is the highest in the world (60.7 cases per 100,000 in 2008).²³ The higher incidence in these countries is because of a combination of factors including diet, lower screening thresholds, and more accurate pathologic staging of the disease.^{24,25} Cases of GC in the West tend to present at more advanced stages, shifting the focus of treatment toward neoadjuvant therapy and away from improving techniques for resection.²⁶

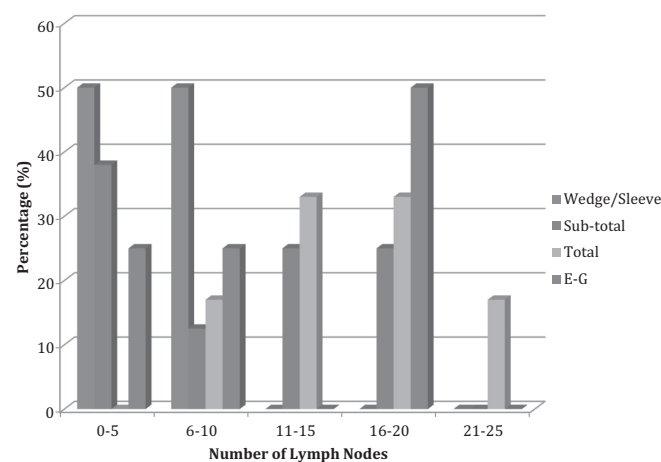


Figure 2. Lymph node harvest by procedure, showing the percentage of each procedure during which a given number of lymph nodes were retrieved. E-G = esophagogastrectomy.

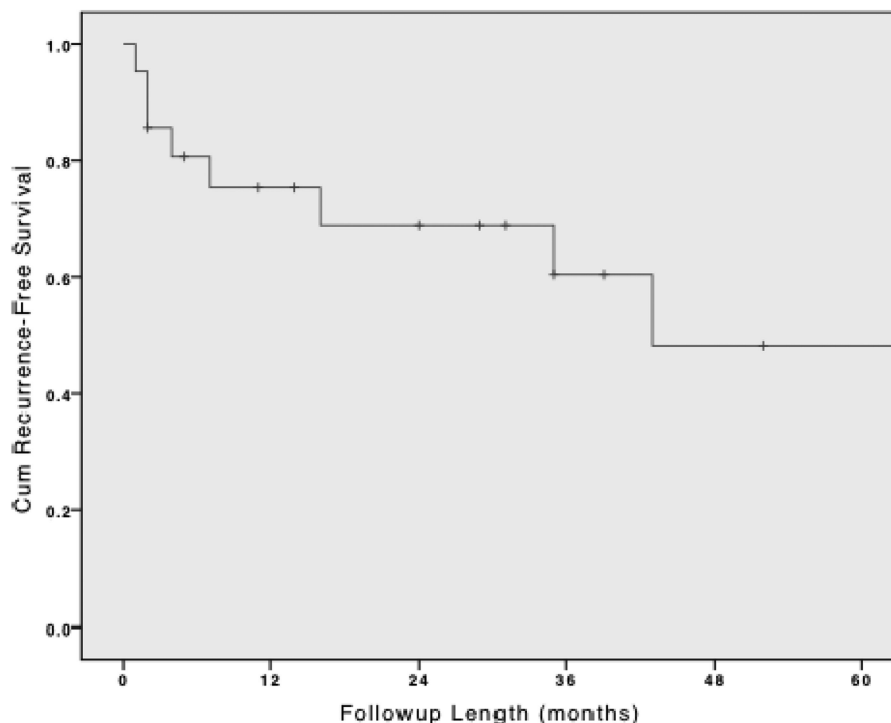


Figure 3. Kaplan-Meier 5-year overall survival and disease-free survival for cases of adenocarcinoma. Cum = cumulative.

At present in the United States, laparoscopic wedge resection for low-grade malignant tumors (GIST) and early-stage adenocarcinoma is a standard procedure.^{27,28} Laparoscopic subtotal gastrectomy and total gastrectomy, though performed less commonly, are becoming endorsed as legitimate alternatives to open surgery. Studies of LA gastrectomy for GC suggest comparable rates of morbidity and mortality, as well as similar oncologic outcomes.^{12,14,29} Although an adequate lymph node dissection according to the AJCC remains 15 nodes, the prognostic advantages of a D2 over D1/D0 dissection remain unclear.^{21,30} Japanese surgeons continue to use an extended lymph node dissection for all patients with at least a T1 tumor containing submucosal invasion.⁸ Evidence for this practice is based mainly on nonrandomized trials suggesting a survival benefit in patients with N2 nodal disease.³¹ There is a lack of level I evidence from Western studies to show the benefit of a D2 dissection.³² This is possibly because of high morbidity and mortality rates not seen in high-volume areas such as Japan, thereby limiting the application of D2 dissection in this population.³⁰

The early experience of our institution in applying laparoscopic techniques for resection of GC has been consistent with the literature, showing morbidity and mortality rates similar to those of recent Western studies.^{13,33–35} The

presence of positive surgical margins in several cases is a reflection of the extent of disease present in our patient population; all cases of adenocarcinoma with positive margins involved emergent cases or patients with linitis plastica with tumor extension into adjacent structures. The number of lymph nodes acquired during dissection was less than recommended by the AJCC.²¹ D2 lymphadenectomies at our institution are performed only in the event of advanced disease or bulky lymphadenopathy noted intraoperatively. For this reason, cases of early-stage adenocarcinoma were most commonly found to have fewer harvested lymph nodes than cases of more advanced GC. Despite the harvesting of fewer lymph nodes, the survival rate observed in this series remains comparable with other Western studies.⁴

Several trials comparing outcomes of laparoscopic and open gastrectomy in GC show the advantages of laparoscopic techniques.^{36,37} Although this was not a comparative study, the benefits of a minimally invasive approach were also suggested in our patient population. The estimated blood loss, length of stay, and narcotic use in this series were comparable with data reported in the current literature.^{1,38,39} The average operative time in this study was also noted to be shorter than expected given a projected learning curve of ≥ 50 cases for LA distal gastrectomy.^{22,40}

Most published data addressing laparoscopy in GC describe LA gastrectomy. There are few that use a totally laparoscopic approach. Moisan et al³ reported on a matched-cohort study involving 62 patients, of whom 31 underwent a TLG. Their study excluded patients with an R1 or R2 resection, those with a lymph node dissection of less than D1, and those with pathology other than adenocarcinoma.³ Strong et al⁷ used a totally laparoscopic technique while performing subtotal gastrectomies. Our study included all gastric malignancies and associated totally laparoscopic resections.

The 5-year survival data presented in this study were similar to other Western series of LG and to outcomes of open gastrectomy.^{3,33,41} Large Japanese studies have shown superior survival rates, yet these mainly reflect the findings of early GC treatment in a high-volume population.⁸

There are several limitations to our study. Because we focused on our experience in laparoscopy only, there was no comparison with data from open gastrectomy for GC at our institution. Our study was performed retrospectively, and the data collected were not randomized and may have been subject to associated bias. Given the long study period, standards of care as well as technology have improved, possibly affecting our results. Randomized, prospective clinical data are needed to further evaluate the applicability of these results.

CONCLUSION

This retrospective study shows that TLG for the treatment of GC is a feasible option with acceptable 5-year survival and perioperative outcomes. Its oncologic equivalency will be better determined as long-term survival data become available. Larger randomized trials are still needed to guide recommendations concerning the totally laparoscopic approach for patients with advanced disease.

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