Early experience of laparoscopic-assisted distal gastrectomy in resectable advanced gastric cancer: a single-center analysis

Mahmoud A. Shahin, Mohamed H. Elmelegy, Hady Saleh Abou-Ashour

Department of General Surgery, Faculty of Medicine, Menoufia University Hospital, Menoufia, Egypt

Correspondence to Hady S Abou-Ashour, MD, MRCS, Department of General Surgery, Faculty of Medicine, Menoufia University Hospital, Menoufia 32951, Egypt.
Tel: +20 106 400 8666;
e-mail: drhadyabouashour@gmail.com

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Background
Although laparoscopic gastrectomy has been in use for more than 20 years, there was great suspicion for its technical feasibility, ability to achieve successful reconstruction of the digestive tract, and oncological safety. However, with recent advancements of laparoscopic surgical instruments and the accumulation of operative experience, laparoscopic gastrectomy becomes more feasible.
Objective
The study was designed to present our initial experience of laparoscopic-assisted distal gastrectomy.
Patients and methods
This was a single-center study. Data was recorded and retrospectively analyzed from September 2017 to August 2022. All patients were admitted for gastrectomy of proved distal gastric malignancy through our outpatient clinics at Menoufia University Hospital were evaluated for eligibility. Cases of emergent operation and obvious locally advanced disease were excluded, and 32 cases underwent laparoscopic-assisted distal gastrectomy.
Results
The study consisted of 21 (65%) male and 11 (35%) female patients, with a mean age of 57±11 years (range, 45–77 years). Mean operative time was 220±19 min (range, 185–255 min). The amount of blood loss was about (200±96 ml). Clear fluids were started 72 h after surgery and soft diet allowed after 4 days. The mean length of the hospital stay was 7.7 days.
Conclusion
In selected patients, laparoscopic gastrectomy is a safe, feasible, respectable option, and an effective method and is oncologically comparable to open gastrectomy for our center.

Keywords:
advanced gastric cancer, distal gastric cancer, laparoscopic distal gastrectomy

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Introduction

Although its prevalence has dropped over the past 10 years, gastric cancer is the third most common cause of cancer-related deaths globally and the fifth most widely spread cancer [1]. The mortality and disease-free survival of patients with gastric cancer seem to be improved due to multimodality treatment, neoadjuvant chemotherapy, R0 surgical resection and sufficient lymphadenectomy, postoperative adjuvant chemotherapy, and radiation [2].

Men worldwide have a gastric cancer rate that is around double that of women. When diagnosed, most patients are in the old age group. Based on how closely it adheres to the long axis of the stomach, the location of gastric cancer is categorized. A little more than 40% of malignancies start in the lower portion of the organ, followed by 40% in the middle, 15% in the upper region, and 10% affecting more than one part of the stomach [3].

The number of patients receiving laparoscopically assisted gastrectomy (LAG) treatment has progressively grown since laparoscopy-assisted distal gastrectomy (LADG) with lymph node dissection for early gastric cancer introduced in 1994 in Japan [4]. Currently, proximal, complete, and LAG procedures are available in addition to distal gastrectomy [5].

Surgery for advanced gastric cancer (defined as T2-4aN0-3M0, corresponding to stages Ib–IIIc excluding T1 or T4b tumors; American Joint Committee on Cancer Staging Manual) is technically more difficult because D2 lymph nodes must be dissected. This is in contrast to surgery for early-stage gastric cancer.

Laparoscopic techniques may not allow for adequate D2 lymphadenectomy [6].

Patients who had LAG experienced less pain, quicker return to active daily life, shorter hospital stays, and greater quality of life than patients who received standard open surgery, according to several small retrospective studies reporting the short-term result of LAG [7,8]. The enlargement of the field of view provided by laparoscopy allows for a more thorough dissection of the lymph nodes, which is advantageous for the patient's prognosis [9]. However, because to the paucity of extensive study data on the short-term and long-term effects, LAG for the treatment of cancers remains debatable.

While several randomized controlled trials (RCTs) and meta-analyses have been published for patients with early gastric cancer, there have only been a limited number of studies done for patients with advanced gastric cancer, most of which are smaller scale and primarily retrospective [10]. All the randomized clinical studies were carried out in large volume locations like China, Korea, and Japan, where the outcomes are frequently better [11]. Laparoscopic distal gastrectomy (LDG) and open distal gastrectomy exhibited equal postoperative morbidity and survival rates in the Chinese Laparoscopic Gastrointestinal Surgery Research (CLASS)-01 trial in China [12], the JLSSG 0901 study in Japan [13], and the Korean Laparoscopic Surgical Society (KLASS)-02 study in Korea [11].

Patients and methods

Design

In all, 32 patients with distal gastric cancer underwent laparoscopic-assisted D2 gastrectomy between September 2017 and August 2022 for the purpose of this prospective and retrospective study. Retrospectively, 10 patients were included, and prospectively, 22 patients were included. Every patient signed an informed consent. The following were the inclusion requirements: preoperative gastroscopy and abdominal computed tomography revealed a pathologically confirmed adenocarcinoma of the stomach, advanced gastric cancer (defined as T2-4aN0-3M0, corresponding to stages Ib–IIIc excluding T1 or T4b tumors; American Joint Committee on Cancer's AJCC Cancer Staging Manual); patients who underwent neoadjuvant chemotherapy and shown a satisfactory response (>30% reduction in tumor size) in accordance with the Response Evaluation Criteria In Solid Tumors (RECIST) criteria 1.1 for T3 or T4 tumors or those with nodal involvement. Excluded patients were those with metastatic illness, those who had prior upper abdominal procedures, and those with poor performance status.

Upper gastrointestinal endoscopy and computed tomography were regularly performed as part of the preoperative workup. The Eighth Version of the American Joint Committee on Cancer (AJCC) TNM classification was used to define the pathological stage [13].

The study's primary outcome was to assess the feasibility and effectiveness of laparoscopic gastrectomy together with D2 lymphadenectomy in this study.

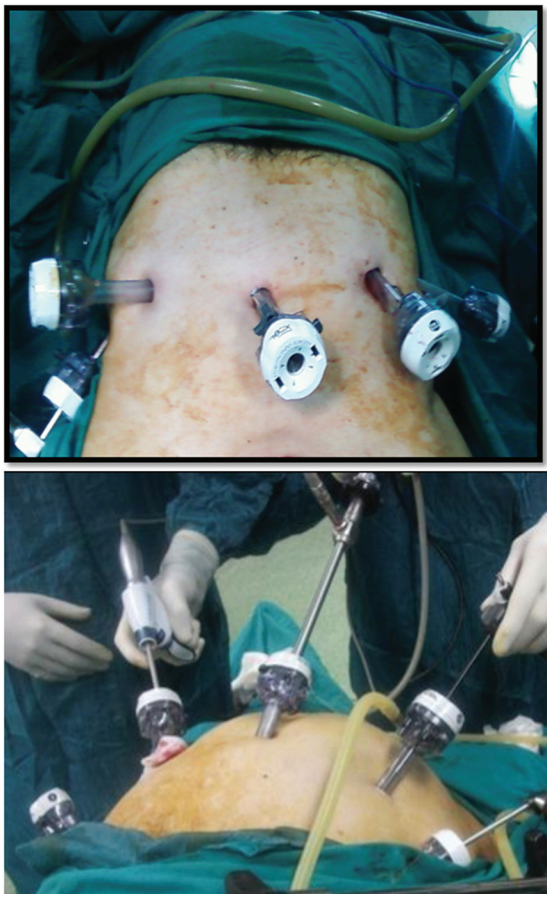
The secondary outcomes included both surgical outcomes and complications of the technique and oncologic outcomes. Surgical outcomes included time of surgery, blood loss, period of hospital stay, time for oral intake, and intraoperative and postoperative (≤30 days) morbidities and mortalities were assessed. The secondary oncologic outcomes were number of harvested lymph nodes, histopathological data, and both distal and proximal resection margins.

Procedure

The principles of the D2 lymph node dissection and the extent of the LDG were followed in accordance with the Japanese recommendations. For lymph node dissection and diagnostic tumor staging, we typically employed five trocars, and for specimen retrieval and anastomosis, a mini-laparotomy was performed. The use of the ultrasonic scalpel for dissection and mobilization was adopted. The surgeon's preference and the patient's performance dictated the proper technique for anastomosis.

The open supraumbilical Hasson technique or the Veress needle was used to inflate CO_2 pneumoperitoneum of ~14 mmHg, while the patient was in the reverse Trendelenburg position on their back. The operating surgeon stood between the patient's legs, a camera assistant on the right side, and the assistant surgeon on the left. Figure 1 illustrates the typical placement of two 12 mm laparoscopic trocars: one supraumbilical trocar for the laparoscope, one in the left midclavicular line at the intersection with the transverse umbilical line, one 5 mm or 10 mm port at the contralateral site, and one 5 mm trocar in the right subcostal area, 2 cm below the costal margin and another 5 mm trocar at the left subcostal region in the anterior axillary line.

Figure 1



Sites of port insertion.

Exploration of the abdominal cavity is the initial stage, which aims to rule out the presence of any preoperatively undetected metastases or peritoneal seeding. A laparoscopic energy device (typically ultrasonic shears; Ultracision-Harmonic Scalpel, Ethicon Endo-Surgery Inc., Cincinnati, Ohio, USA – or radiofrequency device; LigasureTM Instrumets Covidien, Medtronic, Minneapolis, Minnesota, USA) was used to perform the dissection after the neoplasm's effective resectability was established.

According to the Japanese gastric cancer treatment recommendations (5th ed. and earlier) [2, the D2 lymphadenectomy includes the removal of D1 lymph nodes (stations from no. 1 to 7) and stations 8a, 9, 11p, and 12a].

The procedure basically involved dissecting the left larger omentum to remove it 'en bloc' with the stomach after dividing the gastrocolic ligament at the boundary of the transverse colon. To identify the gastroduodenal artery, which runs between the medial side of the duodenum and the pancreatic head, the right omentum and lymph nodes along the right gastroepiploic vessels (no. 4d) were dissected.

The right gastroepiploic vessels were tied off after Henle's trunk was exposed, and the infra-pyloric lymph nodes (no. 6) were dissected (Fig. 2a). A linear stapler (45 mm or 60 mm endoscopic stapling equipment) was used to transect the duodenum 1–2 cm distally from the pylorus (Fig. 2b).

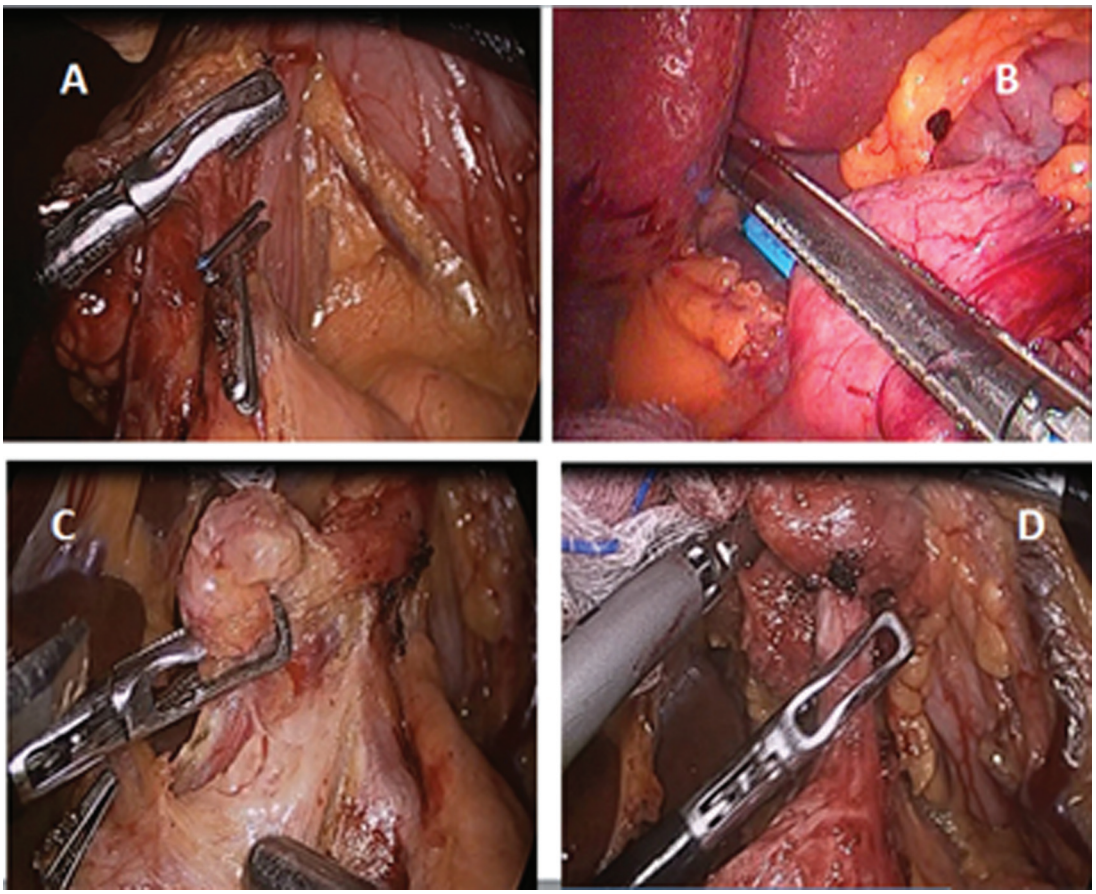
The right gastric artery was revealed and divided at its origin with double clips after the lesser omentum was separated. The supra-pyloric lymph nodes were also divided at this point (no. 5). The excision of lymph nodes from the appropriate hepatic artery (node 12a) and along the common hepatic artery (node 8) followed the incision of the hepato-gastric ligament as the dissection proceeded anterior to the hepatoduodenal ligament (Fig. 2c). The fatty connective tissues around the proximal splenic artery lymph nodes (no. 11p) were also removed.

The stomach was lifted toward the head to expose the gastropancreatic fold as the dissection moved cephalad toward the gastroesophageal junction along the lesser curvature, while concurrently performing a D1 lymphadenectomy of the peri-gastric nodes (no. 3, lesser curvature). Once the esophagogastric junction was reached and the right cardiac nodes (no. 1) approached. Following preparation and separate division of the left gastric vein at the upper border of the pancreatic body, identification of the left gastric artery's root and subsequent double clipping and division at the origin (Fig. 2d), dissection of nodes no. 7 and nodes surrounding the celiac artery (no. 9) was done. An endoscopic linear stapler measuring 60 mm was used to transect the stomach.

The stomach, omentum, and lymph nodes were removed from the resected specimen using a mini-laparotomy (maximum 5–6 cm), typically through upper midline incision (Fig. 3), which must spare muscle, and an Endo catch bag for specimen retrieval was used. Roux-en-Y or Billroth-II method was then used for reconstruction. There were no restrictions on utilizing hand sewing or staplers for anastomosis. Peritoneal drains were typically extracted through trocar orifices and implanted in Morison's pouch, at the gastrojejunostomy site, and in the pelvis at the end of the procedure.

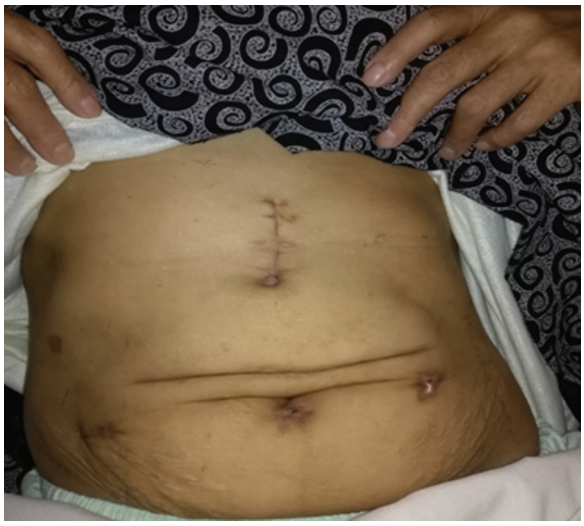
The IBM Corp. (Armonk, New York, USA), statistical analysis was done using IBM SPSS Statistics, version 23. The mean, SD, or median and range, if applicable, were used to express numerical data. The frequency and percentage were used to represent qualitative data.

Figure 2



Operative steps: (a) infra-pyloric dissection, (b) transection of the duodenum, (c) common hepatic artery dissection of lymph nodes, and (d) left gastric artery dissection of lymph nodes.

Figure 3



Scar after specimen extraction 2 weeks postoperatively.

Ethical approval

This research was performed at the Department of General Surgery, Menofia University Hospitals. Ethical Committee approval and written, informed consent were obtained from all participants.

Table 1 Patient demography

Patient characteristics	Values
Age (years) (mean±SD)	47.3±9.7
<50 [*n* (%)]	10 (31)
>50 [*n* (%)]	22 (69)
Sex [*n* (%)]	
Male	21 (65)
Female	11 (35)
Comorbidities [*n* (%)]	20 (62)
DM	4 (16)
HCV + ve	17 (53)
HTN	10 (31)
Neoadjuvant therapy [*n* (%)]	7 (22)

DM, diabetes mellitus; HCV, hepatitis C virus; HTN, hypertension.

Results

Between September 2017 and August 2022, 32 patients had laparoscopically assisted D2 gastrectomy procedures. Table 1 contains the characteristics of the

Table 2 Pathological data of the tumor

Pathological data	Value
Number of retrieved lymph nodes (median)	29 (13–51)
Adequacy of lymph node yield [*n* (%)]	
> 15	28 (94)
< 15	2 (6)
Positive proximal surgical margin [*n* (%)]	0
Positive distal surgical margin [*n* (%)]	1 (3)
T stage [*n* (%)]	
p T2	17 (53)
p T3	10 (31)
p T4a	5 (16)
N stage [*n* (%)]	
p N0	7 (22)
p N1	13 (41)
p N2	8 (25)
p N3	4 (12)
TNM stage (AJCC 8th Edition) [*n* (%)]	
IB	3 (9)
IIA	10 (31)
IIB	12 (38)
IIIA	4 (12)
IIIB	3 (9)

AJCC, American Joint Committee on Cancer.

patients. Their mean age was 47.3±9.7; the study included 11 (35%) female patients and 21 (65%) male patients (range, 39–65 years old).

In Table 2, the histopathological information is displayed. The AJCC classification (8th edition) indicated that three (9%) patients, 22 (69%) patients, and seven (22%) patients were in stages II and III, respectively. The median number of lymph nodes that were retrieved was 29 (between 17 and 51), while the median number of lymph nodes that were positive was nine (range, 3–20). Lymph nodes were positive in a total of 20 (62%) patients and negative in 12 (38%) individuals.

Patients started oral fluids after a median duration of 5 days; the median estimated blood loss was 200 ml (range, 150–300 ml); the median hospital stay was 8 days (range, 6–15); and the median operating time was 220 min (range, 185–275 min) (3–7). In six (18%) patients, conversion to an open laparotomy was necessary. Bleeding, which happened in three individuals, was the primary factor in conversion. Other factors that contributed to conversion were adhesions, the mass's adherence to the pancreatic head, and technical difficulties (failure to fire the stapler).

The average postoperative hospital stay was 7.7 days, but it might have been as long as 13. Two patients underwent revision surgery, one for anastomotic leakage and the other for duodenal stump leaking, as shown in Table 3.

Table 3 Operative and surgical details

Variables	Values
Operative time (min) [median (range)]	220 (185–275)
Blood loss (ml) [median (range)]	200 (150–300)
Hospital stay (days) [median (range)]	7.7 (5–13)
Start oral fluids (days) [median (range)]	5 (3–7)
Conversion to open procedure [*n* (%)]	4 (12)
Bleeding [*n* (%)]	1 (3)
Mass was adherent to the pancreatic head [*n* (%)]	2 (6)
Failure to fire the stapler [*n* (%)]	1 (3)
Reconstruction [*n* (%)]	
Billroth II	26 (81)
Roux-en-Y	6 (19)
Postoperative complications [*n* (%)]	4 (12)
Reoperation [*n* (%)]	2 (6)
Anastomotic leakage	1 (3)
Duodenal stump leakage	1 (3)

According to Table 3, the overall rates of postoperative morbidity and death for all patients were 12% (four instances) and 3% (one case), respectively. Anastomotic leakage, duodenal stump leaking, wound infection, and intra-abdominal abscess were among the surgical problems that affected four patients. Two patients who experienced postoperative deep vein thrombosis and one who suffered a myocardial infarction both had nonsurgical complications. One death from septicemia due to duodenal stump leaking was documented in the postoperative phase (after 12 days).

Discussion

Patients with resectable gastric cancer are currently advised to undergo distal gastrectomy with D2 lymph node dissection. Laparoscopic techniques have gained popularity as a result of developments in minimally invasive surgery throughout time [14].

Laparoscopic-assisted distal gastrectomy, which is now the standard of care for early-stage gastric cancer in Asian nations like Japan and Korea, has level III evidence that surgery is technically safe and has superior short-term results than traditional open gastrectomy [15].

Before the procedure may be generally advised, it must be proven to be safe and oncologically adequate for treating advanced gastric cancer. The main issues here are whether the lymphadenectomy was effective, if the stomach resection was appropriate (particularly after

total gastrectomy), and whether the reconstruction could be finished [16].

Only a small number of studies have reported the outcomes of laparoscopic D2 gastrectomy, even though several studies have compared LAG with traditional open surgery. One of the most significant was the multicenter RCT KLASS-02 [17] that the KLASS group started in 2015. They have shown benefits in terms of short-term outcomes (lower complication rate, quicker recovery, and less pain compared with open surgery) [11] and a comparable 3-year relapse-free survival rate with respect to open distal gastrectomy (ODG) [17].

In Korea (COACT1001 study), comparable multi-institutional prospective RCTs comparing LADG with ODG for localized advanced gastric cancer were undertaken [15,18]. This study demonstrated no significant difference in the overall postoperative complication rate between LADG and ODG, in addition to a compliance rate of D2 lymph node dissection that was the same, so establishing the oncologic sufficiency of LADG in addition to its safety. The CLASS Group carried out a multicenter RCT study (CLASS-01) using a similar design to the Korean group [12].

Initial operating times in this trial were found to be around 275 min, which is more than double the times recorded for skilled surgeons doing a traditional open gastrectomy. By the end of the research, the time was reduced to roughly 185 min The mean operative time in this study (220 min) was quite close to that of previous investigations, such as the study by Lee *et al.* [17] in Korea, which showed a mean operating time of 227 min. In addition, this period of time is close to that of the Chinese research (CLASS-01 trial) [10], which showed a mean operating period of 217 min.

The prolonged time of the surgical procedure is brought about by the need to change the equipment, clean the camera, completing a mini-laparotomy, performing the anastomosis, and then inserting drains [16]. However, our study's operating time was shorter than studies that were done in Japan (JCOG0912 trial) and Korea (COACT 1001 trial), where the mean surgical times were 278 and 257.4 min, respectively [13,15]. This may be explained as most of our anastomoses (81%) are Billroth II technique not Roux-en-Y anastomosis or Billroth I. One of the key advantages of laparoscopic surgery over open surgery is the reduction of blood loss caused by the quick identification and management of tiny capillaries. According to earlier studies, the expected blood loss for a complete laparoscopic gastrectomy varied from 82 to 333 ml and 201–440 ml for open operations [19].

The median estimated blood loss in the current study was 200 ml, which is comparable to previous reports. However, compared with previous studies carried out in Korea, China, and Japan, our study is thought to be much higher as regards the amount of blood loss. When Kim *et al.* [9] compared laparoscopic-assisted distal gastrectomy with totally laparoscopic surgery, the mean blood loss was lower (100.5 vs. 117.2 ml); in addition, the mean blood loss was 153 ml in the KLASS-02 trial and was 105 and 115 ml, respectively, in CLASS-01 and JCOG0912 trials [12,15].

Choi and colleagues reported that the retrieved lymph node was significantly greater in the TLDG group than the LADG group (42.6 vs. 46.3, P=0.008), and there were no differences in metastatic lymph nodes between the two groups. The average nodal yield of 29 is less consistent with previously published Eastern studies with retrieved lymph nodes that ranged from 36 to 46 either in total laparoscopic or LAG [20].

In comparison to research in Western nations, such as the study carried out by Brenkman *et al.* [21] in the Netherlands, the median number of extracted lymph nodes in our study was comparable and greater. These results from Asian studies are superior to those studies in Western countries and our study. In addition, seven (22%) patients in our research had had neoadjuvant chemotherapy, which would have affected the quantity of removed lymph nodes. Neoadjuvant treatment caused a decrease in the number of lymph nodes, according to a Chinese research [22].

The 3D high-definition image, which enables the surgeon to dissect the lymphatic tissue along the intricate anatomical structures more clearly and easily, may also help to explain why Asian studies are superior in terms of intraoperative bleeding and the number of harvested lymph nodes. This is especially true in difficult areas like the inferior pyloric area and the superior pancreatic border, where it is simple to reduce intraoperative bleeding [23].

The established standard of care for gastrectomy is the presence of at least 15 lymph nodes in the specimen. Two cases (with 13 and 14 lymph nodes, respectively) in this study had insufficiently collected lymph nodes. However, the overall percentage for whom sufficient

lymph nodes were removed in this rather short research was 30 (94%) out of 32 cases. The R0 resection rate in the current research was 94%, which is superior to a study performed by Brenkman *et al.* [21] that showed an R0 resection rate of 90%. It is, however, adversely comparable to the Korean research, which revealed a 98.1% R0 resection rate [11].

The AJCC has recommended a minimum of 15 dissected nodes since 1997 [24] for an appropriate assessment of N status. Since then, it has been debated how many lymph nodes there actually are. Woo *et al*. [25] in an international retrospective study concluded that improving the retrieval of a maximum of 29 lymph nodes resulted in improved survival. The surgical goal should be this amount of lymph nodes, regardless of the surgical strategy.

According to the current study, patients experienced considerably shorter postoperative hospital stays and earlier oral intake than those who underwent open surgery. When compared with a study in Korea [11], where patients started oral fluids after 3.7 days, patients in our study started oral fluids after a median duration of 5 days (range 3–7). They often used imaging with contrast after 48 h, and the majority techniques were completely laparoscopic, which may help to explain the early oral intake. In addition, this time interval is thought to be shorter than the findings of two studies conducted in China, which reported a waiting interval for oral intake of 5.5 and 5.7 days, but these studies also included patients who had had total gastrectomy. [12,26].

In a research conducted in Korea by Lee *et al.* [17], the total complication rates of open and laparoscopic gastrectomy were 24.1 and 16.6%, respectively. The Chinese Laparoscopic Multicenter RCT research (CLASS-01) [12] over the same recent time period randomized 1056 patients with advanced gastric cancer in 14 Chinese institutions between open and LDG. Despite being insignificant, the morbidity rate in the laparoscopic group (15.2%) was somewhat greater than that in the open group (12.9%). Wang *et al.* [27] and Shi *et al.* [18] reported a greater complication rate in the open compared with the laparoscopic group (LADG 13.1% vs. ODG 17.7%, and 11.72% LAG vs. 14.38% OG, respectively), but the above difference in complication rate was insignificant.

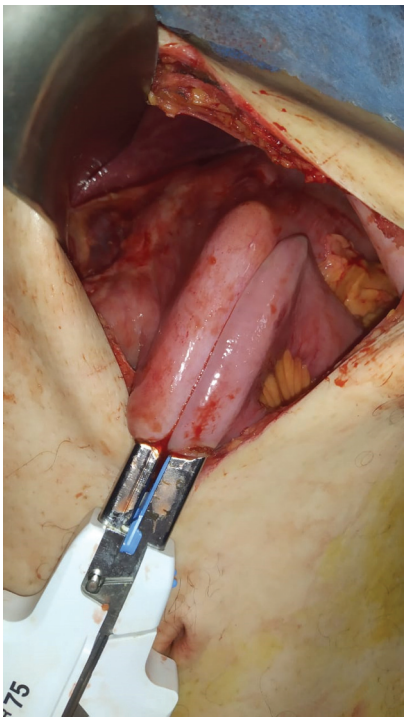
Wang *et al*. [27] reported that postoperative morbidity rates after laparoscopic gastrectomy vary from 6.4 to 24.2%. The morbidity rate in the current study was 12%, which is within the range of previous reports, showing that the complication rate in our study is good.

According to earlier studies, anastomotic leakage rates can range from 0.2 to 14% [11,12]. Anastomotic leakage occurred in one (3%) case in our study, which falls within the range of previous studies. In addition, D2 lymphadenectomy was carried out in all patients in the current study, in contrast to most of the earlier studies where D2 gastrectomy was not frequently carried out.

One of the most serious post gastrectomy consequences is duodenal stump leaking, with rates ranging from 0.4 to 2.4% in previous studies [28–30]. The duodenal stump leakage rate in the current study occurred in one (3%) patient and was 1% higher than the previously published results. This higher rate could be due to the small sample of our study. In this instance, a second procedure was necessary as the patient had sepsis. The stump was reclosed and drains were put in; however, after 12 days the patient passed away of complications. In the current study, intra-abdominal collection was detected in one (3%) patient and was treated with imaging-guided drainage. Katai *et al.* [16] in Japan reported a lower rate of intra-abdominal collection or abscess formation in 1.8% of patients.Pancreatic fistula, however, was not reported in the current study, and its prevalence in previous studies ranged from 0.4 to 1.9% [11,12]. Two (6%) patients, one with duodenal stump leakage and the other with leaking from the anastomotic site, required reoperation. The insertion of drains and a revision of the anastomosis were done after abdominal exploration. Our study's reoperation rate was greater than other studies from China, Japan, and Korea, which showed substantially lower reoperation rates [11,12,15,16]. This is said to be particularly because of the insufficient experience compared with these highly qualified centers with higher rates. However, our study reoperation rate was better than an Italian study which reported a reoperation rate of 9.52% [31].

Conversion to an open procedure is another significant quality indicator in addition to postoperative problems. According to Eastern research, the conversion rate varied between 2.2 and 7% [11,12,32]. Western studies such as Ecker *et al.* [33] and Brenkman *et al.* [21], however, showed conversion rates of 23.9 and 10%, respectively. The conversion rate (Fig. 4) in the current study was 12%, which is significantly higher than that in other studies. However, the reason may be related to our early experience with this difficult technique; the majority of conversions happened in

Figure 4



Conversion to open surgery and gastrojejunal anastomosis.

the first cases and the rate of conversion decreased in subsequent patients. Tumor adhesion to the pancreas, which was found in two (6%) patients, was the primary factor in conversion; the other causes were bleeding in one case and technical difficulty (failure of the stapler) at the duodenal end.

Regarding the learning curve, good patient selection enhanced the learning curve and reduced the conversion rates [34]. In the current study, conversion rates dropped from three conversions in the first 16 (50%) patients to one conversion in the last 16 (50%) patients, and the median lymph node yield increased from 20 lymph nodes in the first 16 cases with two cases having an inadequate lymph node yield (<15 nodes) to 31 lymph nodes in the last 16 patients.

The current study has several limitations. First, as this was a single-center study, bias could be found. Second, a larger sample size is required in order to make a reliable conclusion. Therefore, despite the fact that our study's design is not comparable to those previously reported studies due to its retrospective and prospective nature, lack of randomization, and lack of comparative analysis. We may overcome some of the above discrepancies by sharing of one of our surgeons in these studies by applying for clinical fellowship in the National Cancer Center in Korea and having good learning skills that allowed to be close to the surgical technique and to share it with surgeons who practice advanced laparoscopy in the current study. Despite the above limitations, our results seem to be satisfactory in comparison to the results of former studies.

Conclusion

In selected patients, laparoscopic gastrectomy is a safe, feasible, respectable option, and an effective method and is an oncologically comparable option to open gastrectomy for our center.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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