in another study including patients who underwent open gastrectomy (D1 9.4 %; D2 17.8 %) [28]. Apart from the passage of food through the duodenum, destruction of the vagus nerve is also an important risk factor for gallstone formation [29] and such destruction was marked in patients who had undergone extensive lymph node dissection. In a previous study of long-term outcomes, including some patients who underwent pylorus-preserving gastrectomy [30], the incidence of gallstones after ODG was substantially reduced (1.8 %) by preserving the vagus nerve. In the present study, the rate of gallstone formation was 14 %, although the hepatic branch of the vagus nerve was preserved in all patients and the celiac branch was preserved in most. In addition, D2 dissection did not increase the risk of gallstone formation. This apparent discrepancy may be explained by the following factors. Gallbladder function is regulated not only by the hepatic branches of the vagus nerve, but also by the retroperitoneal sympathetic and parasympathetic nerves [29]. When D1 + α or D1 + β lymph node dissection was performed in the present study, part of the nerve plexus along the common hepatic artery or the celiac artery might have been damaged by complete dissection of the No. 8a or No. 9 lymph nodes. Furthermore, ultrasonically activated devices were mainly used to perform lymph node dissection, and heat generated at the time of dissection might have injured the preserved nerves. No patient in the present study had symptomatic cholecystolithiasis or received treatment for gallstones. In contrast, a previous study reported that cholecystolithiasis developed in 27 % of patients with gallstones after open gastrectomy, and 46 % of these patients received surgical treatment [28].

The reconstruction method of choice after LDG remains controversial. B-I and R-Y procedures are the most widely used. Some reasons for favoring B-I may be its technical ease and the maintenance of digestive-system-related homeostasis and food flow into the duodenum. However, the passage of food through the duodenum may not be an important determinant of nutritional status after distal gastrectomy. Nutritional indexes such as serum albumin levels, serum total cholesterol levels, and body weight are similar after R-Y and B-I in the short term [15, 20], as well as in the long term, as demonstrated by the present study. Consistent with the results of our previous study, these nutritional indexes were similar in the R-Y and B-I groups in the present study at 6 months, 1 year, and 5 years after the operation. The size of the remnant stomach was an important determinant of the quality of life after gastrectomy. In another study [31], a larger remnant stomach after distal gastrectomy was associated with benefits such as less reflux esophagitis, more stable body weight, and better food intake in the B-I group. In patients with cancer arising in the lower third of the stomach, a larger remnant stomach can improve nutritional status and reduce symptoms [31]. We did not accurately measure the size of the remnant stomach in our series, but the upper third of the stomach was preserved in most patients. The size of the remnant stomach was less than one half in all patients. In patients in whom tension on the gastrointestinal anastomosis was a concern, the remnant stomach was slightly larger than the upper-third portion. As for late gastrointestinal complications, ulcers developed only after B-I in the present study. Stomal ulcer is a concern in R-Y because of less alkaline bile reflux into the stomach, potentially leading to acid-induced jejunal injury [32]. However, to avoid excessive tension on the gastroduodenostomy, the size of the remnant stomach might be larger and, consequently, acid production might be higher in B-I. On the other hand, the incidence of ileus was higher in the R-Y group in our study. Internal hernia after R-Y has been reported in patients who underwent gastric bypass surgery or LDG [33, 34]. One patient (1.2 %) in our R-Y group had an internal hernia, as compared with no patients in the B-I group. Mesenteric defects, including Petersen's defect, should be closed in LDG, as is done in R-Y gastric bypass surgery [34]. Roux stasis syndrome is characterized by symptoms of upper gut stasis after R-Y gastrojejunostomy and is thought to be caused by an ectopic pacemaker that arises in the proximal part of the Roux limb divided from the natural small bowel pacemaker [35]. However, Roux stasis syndrome was not diagnosed in any of our patients for 5 years after the operation, although two patients (2.4 %) had disturbed food passage associated with an expanding remnant stomach and a bent Roux limb during the early postoperative course. Roux stasis syndrome has been attributed to removal of the vagus nerves and the length of the Roux-Y limb [36, 37]. We decided to use a Roux limb less than 30 cm in length on the basis of the results of previous studies [37]. Endoscopy for the papilla of Vater, or endoscopic retrograde cholangiopancreatography was impossible in R-Y. However, balloon enteroscopy is useful for these examinations [38]. Remnant gastric cancer (RGC) is also an important issue after gastrectomy. Patients in whom reconstruction is performed with B-II procedures at the first operation have the highest risk of RGC. The development of RGC is attributed primarily to duodenogastric reflux and hypochlorhydria [39]. R-Y may decrease the risk of secondary gastric cancer, but further long-term follow up is necessary to reach a definite conclusion on this risk. Low incidences of RGC have been reported after R-Y reconstruction, because B-I or B-II has been the main method employed [39, 40].

In conclusion, as compared with B-I, R-Y was associated with lower long-term incidences of both bile reflux into the gastric remnant and reflux esophagitis. Late complications and nutritional status did not differ between the R-Y and B-I groups.

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ORIGINAL ARTICLE

A prospective feasibility and safety study of laparoscopy-assisted distal gastrectomy for clinical stage I gastric cancer initiated by surgeons with much experience of open gastrectomy and laparoscopic surgery

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Abstract
Background The aim of this prospective study was to evaluate the feasibility and safety of laparoscopy-assisted distal gastrectomy (LADG) initiated by surgeons with much experience of open gastrectomy and laparoscopic surgery.
Methods Three surgeons who each had experience with more than 300 cases of open gastrectomy, more than 100 cases of laparoscopic cholecystectomy, more than 5 cases of laparoscopic colectomy, and more than 5 cases of laparoscopic partial gastrectomy were nominated as LADG operators. All three operators received training for LADG with study materials including videotapes, a box simulator, and an animal laboratory, with lectures and assistance from LADG instructors who each had experience of more than 50 LADG operations. Then the nominated LADG operators performed LADG with the instructors, in which their skills were evaluated and certified. Thereafter, they performed LADG without assistance from the instructors. The target of this study was clinical stage I gastric cancer that was resectable by distal gastrectomy. D1 + alpha, D1 + beta, or D2 dissection was performed laparoscopically. Basically reconstruction was done extracorporeally with a Billroth-I gastroduodenostomy. An extramural review board checked the surgical quality of the operations performed by the three surgeons. The primary endpoint was morbidity and mortality.
Results A total of 193 patients were enrolled in this study between August 2004 and July 2009. The median blood loss was 35 ml and the median operation time was 250 min. Conversion to open surgery was seen in 6 patients; 4 due to bleeding and 2 due to advanced disease. Overall morbidity was 1.6 %, including grade 2 anastomotic leakage in 0.5 % and grade 2 pancreatic fistula in 0.5 %. No mortality was observed. The number of cases required until the LADG operators acted as LADG surgeons without an instructor was 3 for each of the three surgeons. When comparing the data between that in the training period ($n = 9$) and the operators' data ($n = 174$), the median operation time was significantly longer in the training period (355 min) than in the latter period (247.5 min) ($p = 0.015$). Median blood loss was also greater in the training period (150 ml) than the latter period (32.5 ml), but the difference did not reach statistical significance ($p = 0.084$). During the training period, no patient developed any complications of $\geq$grade 2.
Conclusion These results suggested that LADG could be initiated and performed feasibly and safely if surgeons with much experience of open gastrectomy and laparoscopic surgery received adequate training for LADG.

Keywords Laparoscopy · Gastrectomy · Prospective study · Gastric cancer

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Introduction

Early gastric cancer is a highly curable disease; thus, there is an increasing demand to improve patients' postoperative quality of life. Kitano first reported laparoscopy-assisted distal gastrectomy (LADG) in 1994 [1]. Initially, the feasibility and safety were not satisfactory [2]. However, several studies have recently demonstrated that LADG is feasible, safe, less invasive than open surgery, and yields good quality of life in addition to having cosmetic benefits [3–6]. Moreover, long-term survival has been evaluated in a retrospective analysis of a case series with a large sample size [7]. Recently, Katai et al. [8], in a phase II study, reported an incidence of 1.7 % each for pancreatic fistula and anastomotic leakage . Based on this finding, they initiated a phase III trial for early gastric cancer to show that the survival of LADG was comparable to that of conventional open distal gastrectomy. Moreover, another phase II/III trial for resectable advanced disease has been launched by a group of leading Japanese laparoscopic surgeons. However, these phase III trials have been performed only by experienced, specifically accredited surgeons.

It may be difficult to expand the application of LADG in Japan if the phase III trials are found to have positive results, because most surgeons in this country have no experience of LADG. However, Japanese surgeons in general hospitals have much experience of open gastrectomy for gastric cancer, and they are also experienced in performing laparoscopic cholecystectomy. Some surgeons have experience of laparoscopic partial gastrectomy and may have experience of colectomy with nodal dissection for colon cancer. Many surgeons would have experience with the use of ultrasonic cutting and coagulating systems when dissecting lymph nodes in open or laparoscopic surgery, opening the omentum in staging laparoscopy, or removing the lesser curvature in laparoscopic partial gastrectomy. Furthermore, as laparoscopic surgery is easily recorded by videotape, this enables surgeons to learn the skill more quickly and efficiently. Although LADG is a technically complex procedure, each part consists of a basic technique. If surgeons have enough experience of gastric cancer surgery and laparoscopic surgery, the performance of LADG might be only a small next step. The aim of the present study was to evaluate whether surgeons experienced in the procedures outlined above could initiate and perform LADG safely and feasibly.

Patients and methods

Eligibility criteria

The eligibility criteria for this study included: (1) histologically proven gastric adenocarcinoma; (2) T1N0, T1 with nodal metastases limited to the perigastric nodes, or T2N0 clinically determined by endoscopy and abdominal computed tomography (CT) scan, according to the the Japanese Gastric Cancer Association (JGCA) *Japanese classification of gastric carcinoma, 2nd English edition* [9]; (3) curative surgery that could be performed by distal gastrectomy; (4) no distant metastases, clinically confirmed by physical examination, chest X-ray, and abdominal CT scan; (4) Eastern Cooperative Oncology Group (ECOG) performance status 0–1; (5) sufficient organ function (according to laboratory data, and physically able to tolerate surgery); (6) forced expiratory volume in 1 s of $\geq$50 %, expected vital capacity of >70 %, and arterial oxygen pressure in room air of $\geq$94 torr); and (7) written informed consent. Exclusion criteria included: (1) previous history of upper-abdominal surgery; (2) lower-limb varicose veins needing treatment; (3) presence or previous history of deep vein thrombosis; and (4) uncontrolled arrhythmia, or cardiac disease even when controlled with medication.

Surgery

Five or six ports were used. Lymph node dissection was performed in the laparoscopic field. The omentum was preserved except where resection was necessary for lymph node dissection along the right gastroepiploic artery. A small abdominal incision (<7 cm) was made for removal of the specimen and reconstruction. Reconstruction was done with Billroth-I gastroduodenostomy, in principle, but Billroth-II or Roux-en Y gastrojejunostomy was applied for small remnant stomachs. All the reconstruction procedures were performed extracorporeally with circular staplers.

The minimum extent of dissection was determined by the JGCA guidelines [10]. Briefly, the details of nodal dissection and indications were: (1) D1 with nodal dissection along the left gastric artery (#7) and the common hepatic artery (#8a), termed D1 + alpha, is indicated for mucosal tumors with a diameter of <1.5 cm with differentiated histology; (2) D1 + alpha with nodal dissection around the celiac artery (#9) is indicated for T1N0 tumors that do not fulfill the indications for D1 + alpha, and this procedure is termed D1 + beta; and (3) D2 dissection, which is indicated for T1 with nodal metastases limited to the perigastric nodes, or T2N0 tumors. Nodal dissection was done laparoscopically. Conversion to open surgery was permitted when nodal metastases were found along the major branched arteries or serosal invasion by the tumor was suspected during laparoscopic surgery.

LADG was defined as follows: (1) lymph node dissection was performed laparoscopically and (2) mini-laparotomy of 7 cm was permitted only for reconstruction. Any surgery which did not fulfill the criteria for LADG was defined as open surgery.

Participants and quality control of surgery

Three hospitals (Kanagawa Cancer Center, Yokohama City University Hospital, and Kanagawa Ashigawa-Kami Hospital) participated in this study. Only three surgeons (T. Yoshikawa, Y. Rino, and Y. Yamamoto), one at each hospital, were responsible for LADG. Each of the three surgeons had experience of more than 300 cases of open gastrectomy, more than 100 cases of laparoscopic cholecystectomy, more than 5 cases of laparoscopic colectomy with lymph node dissection for colon cancer, and more than 5 cases of laparoscopic partial gastrectomy for small submucosal tumors, but none of the three had experience with LADG. All three surgeons had been certified both by the Board of the Japan Surgical Society and by the Japanese Gastroenterological Society. Each surgeon nominated several attending surgeons who could be assistants with LADG. The attending surgeons each had experience of more than 50 cases of open gastrectomy and more than 20 cases of laparoscopic cholecystectomy, but no experience of LADG. These attending surgeons had been certified by the Board of the Japan Surgical Society. They received the following first, second, and third training modules with the above three surgeons, and participated in LADG as laparoscope operators or assistants.

Another two surgeons (T. Fukunaga and M. Kimura), who had LADG experience of more than 50 cases, were invited from other hospitals to act as instructors. The training system was as follows: the first step was to learn how to use the laparoscopic instruments and how to create and show the surgical field; for this training the instructors gave lectures using a videotape that was shown many times. The second step was to use the laparoscopic instruments in a box simulator, in the same way as that shown in the videotape, without the instructors. The third step was to perform a gastrectomy in the animal laboratory in the same way as that shown in the videotape, with lectures and assistance from the instructors. The fourth step was to perform the surgery for gastric cancer patients with assistance from the instructors. The instructors evaluated the trainee's skills and judged whether they could perform LADG surgery without instructors. The fifth step was to perform the surgery without assistance from the instructors. All surgical procedures were recorded on videotape.

An extramural review board, with members having expertise in open surgery for gastric cancer (Dr. M. Ninomiya of the Department of Surgery, Hiroshima City Hiroshima Hospital, Hiroshima, Japan and Dr. N. Hirabayashi of the Department of Surgery, Hiroshima City Asa Hospital, Hiroshima, Japan) checked the videotapes of the operations on the patients. A score sheet was used to evaluate the surgical skills in reconstruction and in dissection by separating each lymph node station. Briefly, the skill was scored as almost perfect (100 %), good (80 %), acceptable (60 %), inappropriate (40 %), and unacceptable (20 %). Mean scores for dissection and reconstruction were calculated separately. If the mean scores were <60 %, such operators were not permitted to do LADG.

Objectives and statistical hypothesis

The objective of this study was to evaluate the feasibility and safety of LADG. The primary endpoint was surgical morbidity and mortality. Key secondary endpoints were the number of harvested lymph nodes, blood loss, operating time, and overall survival. Surgical morbidity and mortality were evaluated by the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0 [11] until 3 months after discharge. Long-term morbidity requiring admission was not evaluated in this study. Data were collected from the first case of surgery with the instructors and were analyzed all together. The safety and feasibility were evaluated in all cases including the training period, because the target was early gastric cancer, which has a high curability rate with open surgery.

The accrual period was set at 5 years. Feasibility and safety were evaluated in the patients enrolled in this period, and the findings were judged by comparing them with the morbidity and mortality of open distal gastrectomy with lymph node dissection (ODG) as a historical control. Termination of the study was prespecified if three treatment-related deaths occurred before the initial 60 patients were treated.

This prospective study was approved by the local ethics committees at each institution involved. This report presents the morbidity and mortality (which were the primary endpoints) and other surgical results, including number of harvested lymph nodes, blood loss, and operating time, which were the secondary endpoints in this study.

Results

No treatment-related death was observed among the initial 60 patients enrolled. Therefore, accrual was continued for 5 years. A total of 193 patients were enrolled in this study between August 2004 and July 2009. The extramural review board checked the videotapes of representative cases twice during this period. The mean scores for dissection and reconstruction were each more than 70 %.

The background of the patients is shown in Table 1. Only 18 patients had T2 tumors that required D2 dissection. LADG was initiated for all 193 patients enrolled. The surgical results are summarized in Table 2. D1 + alpha dissection was performed in 7 patients, D1 + beta in 163,

Table 1 Patients' background

Sex (M/F)	125/68
Age (years)	
Median (range)	64 (24–83)
Location of tumor	
Middle third (M)	72
Lower third (L)	121
Tumor progression	
Mucosal N0 tumors (diameter <1.5 cm) with differentiated histology	13
Other T1N0 tumors	162
T2N0	18
Body weight (kg)	
Median (range)	57 (37–99)
Body mass index	
Median (range)	22.1 (17.0–34.3)

Table 2 Surgical results

Maximal wound length (cm)	
Median (range)	6 (3.5–18.0)
Lymph node dissection	
D1 + alpha (#7/#8a)	7
D1 + beta (#7/#8a/#9)	163
D2	23
Reconstruction	
Billroth-I	181
Roux-en-Y	12
No. of harvested lymph nodes	
Median (range)	44 (9–114)
Blood loss (ml)	
Median (range)	35 (0–2900)
<500/>500 ml	189/4
Blood transfusion	2
Operation time (min)	
Median (range)	250 (135–595)
Conversion to laparotomy	6
Bleeding	4
Advanced disease	2 (T2N1 in 1 and T2N2 in 1)

and D2 in 23. The extent of lymph node dissection defined by the protocol was maintained in all 193 patients. Most patients received Billroth-I reconstruction after distal gastrectomy. The median blood loss was 35 ml and median operation time was 250 min. Conversion to open surgery was seen in 6 patients (3.1 %); in 4 of these patients conversion was due to bleeding that was not controlled laparoscopically and in 2 conversion was due to advanced disease (T2N1 in 1 patient and T2N2 in the other).

Table 3 Pathological findings

Pathological type	
Differentiated/undifferentiated	77/116
T	
T1 (m/sm)	103/71
T2 (mp/ss)	12/6
T3 (se)	1
N	
N0	162
N1 (perigastric nodes)	23
N2 (along major branched arteries)	8
M	
M0	192
M1 (positive peritoneal cytology)	1

m/sm mucosal/submucosal, *mp/ss* muscularis propria/subserosal, *se* serosal

Table 4 Morbidity and mortality

Any complication (≥grade 2)	3 (1.6 %)
Anastomotic leakage	
Grade 2	1 (0.5 %)
Pancreatic fistula	
Grade 2	1 (0.5 %)
Mechanical obstruction	
Grade 3	1 (0.5 %)
Other complications	
≥Grade 2	0
Re-operation before discharge	1
In-hospital mortality	0
Duration of hospitalization after surgery (days)	
Median (range)	9 (7–37)

The pathological findings are shown in Table 3. One patient had advanced tumors invading the serosa, as well as peritoneal cytology. Nodal metastases along the major branched arteries were observed in 8 patients.

The morbidity and mortality data are shown in Table 4. Grade 3 or more morbidity was observed in 1 patient, who had a mechanical obstruction that required surgery. There was no re-operation and no mortality in the 3 months after discharge.

The number of cases required until the trainee surgeons could act as LADG surgeons without a trainer was 3 for each of the three surgeons. When comparing the data between the training period ($n = 9$) and the period when the operators acted without a trainer ($n = 174$), the median operation time was significantly longer in the former period (355 min) than in the latter (247.5 min) ($p = 0.015$). The median blood loss was greater in the former (150 ml) than

in the latter period (32.5 ml), but the difference did not reach statistical significance ($p = 0.084$). During the training period, no patient developed any complications of ≥grade 2.

Discussion

In the present study, the median blood loss was only 35 ml and median operation time was approximately 4 h. Blood loss in ODG is reported to range from 55 to 488 ml, which is slightly more than the present result [12]. The operation time for ODG ranges from 124 to 228 min [12]. Thus, LADG in this study took slightly more time than the reported times for ODG, but the difference was marginal. On the other hand, no mortality was observed in this study, and morbidity was 1.6 %. Moreover, the incidence of pancreatic fistula or anastomotic leakage was only 0.5 %. The rates of anastomotic leakage and pancreatic fistula following ODG are reportedly 0.6–2.7 and 0.6 %, respectively [13–15]. We note that Katai et al. [8] first reported the feasibility and safety of LADG in a large-scale prospective phase II trial in Japan. They demonstrated that the median blood loss was 43 ml and median operation time was 250 min. The incidences of pancreatic fistula and anastomotic leakage were 1.7 % each. The present prospective study showed surgical results that were similar to those in the report by Katai et al. [8]. Thus, the present results suggest that LADG could be initiated and performed feasibly and safely if surgeons with much experience of open gastrectomy and laparoscopic surgery receive adequate training for LADG.

In several case series reported during the initial introduction of LADG, blood loss was reportedly over 200 ml and surgical morbidity was around 10 % [12]. However, surgical results have since improved [8]. LADG has been refined over time. One possible reason is the easy access to surgical skills achieved by using videotapes of procedures, and these can be easily taken during laparoscopic surgery. In addition, technical skills are freely shared during medical and intramural conferences. Improved techniques can be easily spread, and the development of tools has improved techniques. Innovations in cutting tools include an ultrasonic cutting and coagulating system and a bipolar vessel sealing system, which may help to reduce bleeding and shorten the operation time.

The training period in the present study was very short. Only 3 cases were required for each of the three trainee surgeons to be able to be accredited as a LADG surgeon. Although the operating time was longer in the training period than that in the period when the operators no longer required training, no surgical morbidity was observed in the training period. To avoid surgical morbidity such as pancreatic leakage, it is essential to cut along the appropriate line and to separate the correct layer even though it takes a long time. As the three surgeons had much experience with open gastric surgery, they understood the appropriate line along which to cut and the correct layer to separate. Thus, the appropriate surgery could be more important than the operation time when initiating LADG. However, blood loss was slightly high in the training period, which may have been due to the surgeons' immature skills in laparoscopic operation or in stopping the bleeding. As reconstruction was done by an extracorporeal approach in this study, anastomosis-related morbidity was few even in the training period.

According to previous studies, LADG was regarded as a very complicated procedure and surgeons required 50–90 cases to obtain sufficient skills [16–18]. Recently, Mochizuki et al. [19] reported that the minimal number of cases required to obtain sufficient skills was 25 if surgeons had strict surgical backgrounds and were well trained. In the present study, the minimal number of cases was only 3. Practical training in the present study was less than that reported by Mochizuki et al. [19]. Their operators did not receive lessons by videotape. Surgical technique can depend on the surgical field, the motion of the instruments, and the method itself. Simulation of surgical technique is possible by videotape without the operator doing practical training. Moreover, the backgrounds of the surgeons in their study were different from those in our study. In their study, the surgeons' only experience of laparoscopic surgery was with cholecystectomy, while the surgeons in the present study had laparoscopic experience with cholecystectomy, partial gastrectomy, and colectomy with nodal dissection for colon cancer. Our results suggested that only several cases were required for surgeons to obtain the skills necessary for LADG if they had sufficient knowledge of gastric cancer surgery, sufficient skill with laparoscopic surgery, and adequate training.

Generally, surgeons begin with an easy operation and go forward to the next step. Experience with laparoscopic surgery would be similar. Circumstances around surgery in general hospitals have changed dramatically from the time when the technique of LADG was first developed. The technique of LADG is now established and sophisticated. The instruments have been improved. Basic laparoscopic surgery is performed widely in Japan. The employment of laparoscopic colectomy is also spreading. Before initiating LADG in general hospitals, surgeons may now have experience of laparoscopic cholecystectomy, laparoscopic partial gastrectomy, and laparoscopic colectomy. Thus, in the present study, the backgrounds of the surgeons may be much closer to those in current circumstances in general hospitals compared with the backgrounds of the surgeons in Mochizuki's report [19]. Although our study achieved

excellent results, it is still unclear whether our methods are applicable to other surgeons with similar surgical backgrounds. A confirmatory study is necessary.

There are several reasons for the excellent results of the present study: first, the surgeons had much experience of laparoscopic surgery. They were used to laparoscopic surgery. Second, the surgeons received adequate step-by-step training. Being able to view a training videotape many times is extremely important for learning about the surgical field and work of the instrument. Only after obtaining the image of LADG were surgeons trained to do the same work in the surgery. Third, surgeons who had much experience of LADG acted as instructors. It usually requires an extended period to improve and refine surgical skills by practice alone. The instruction by expert surgeons standardized the technique [20, 21], and LADG could be performed correctly for the first patient. All the procedures were checked by the instructors. Fourth, all the responsible surgeons had much experience of open gastrectomy. An understanding of the anatomy and dissection for gastric cancer may help surgeons perform LADG. Moreover, reconstruction was done by an extracorporeal approach following the method developed and standardized in open surgery. All of the surgeons had experience with this reconstruction method. Fifth, the surgical skills were checked by an extramural review board. The surgeons were careful to avoid criticism from the review.

Special attention is required in the interpretation of the present results. There were several limitations of this study. First, there was a possibility of bias in the selection of the patients. This study was a prospective one, performed to evaluate the feasibility and safety of LADG. Only selected patients who satisfied the entry criteria were enrolled in the trial. Moreover, the technique was reviewed by extramural board members. However, some surgeons may have hesitated to operate on elderly or obese patients, or those who had severe co-morbidities even though they satisfied the entry criteria. Therefore, it is unclear whether the present results are applicable to such patients. Second, the trainees in this study had much experience of open gastrectomy and laparoscopic surgery. These methods and results may not be applicable to less experienced surgeons.

In conclusion, LADG could be initiated and performed feasibly and safely if surgeons with much experience of open gastrectomy and laparoscopic surgery received adequate training.

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Clinical Trial Note

Laparoscopic or Open Distal Gastrectomy After Neoadjuvant Chemotherapy for Operable Gastric Cancer, a Randomized Phase II Trial (LANDSCOPE Trial)

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This randomized Phase II trial will compare the efficacy and safety of laparoscopy-assisted D2 distal gastrectomy and open distal D2 gastrectomy after neoadjuvant chemotherapy for patients with macroscopically resectable serosa-positive gastric cancer. When R0/R1 surgery is achieved, patients receive S-1 chemotherapy for 1-year post-operatively. The primary endpoint is the 3-year disease-free survival. The sample size to test the hypothesis of the non-inferiority of laparoscopy-assisted D2 distal gastrectomy to open distal D2 gastrectomy is 80. This trial will be able to appraise the use of the laparoscopic approach as a curative D2 distal gastrectomy after neoadjuvant chemotherapy for gastric cancer.

Key words: gastric cancer – laparoscopy – D2 – gastrectomy – neoadjuvant chemotherapy

INTRODUCTION

Gastric cancer is the second leading cause of cancer death in the world and is the most common malignancy in Japan, South America and Eastern Europe (1). Complete resection is essential for the cure of gastric cancer (2). Even after macroscopic complete resection, more than half of T3 and T4 tumors recur. Recently, adjuvant chemotherapy with S-1 (1 M tegafur–0.4 M gimestat–1 M ostat potassium) for 12 months has been established as the standard treatment after D2 gastrectomy in Japanese patients with Stage II or III disease based on a large Phase III study (3). Nonetheless, even with adjuvant S-1 chemotherapy, the prognosis for serosa-positive tumors was not satisfactory.

Pre-operative (neoadjuvant) chemotherapy followed by extended surgery has some theoretical benefits when compared with post-operative chemotherapy (4). Several European Phase III trials have demonstrated that neoadjuvant chemotherapy, followed by curative surgery and adjuvant chemotherapy, improved the survival for gastric cancer patients (5,6). In Japan, a Phase III trial conducted by the Japan Clinical Oncology Group (JCOG) is now ongoing to evaluate the efficacy of neoadjuvant chemotherapy followed by surgery and post-operative S-1 for clinically resectable scirrhous type gastric cancer. More recently, several regimens and courses of neoadjuvant chemotherapy were tested in clinical T4 or clinical stage III patients in Phase II trials (7).

After neoadjuvant chemotherapy, patients generally receive a D2 gastrectomy with curative intent. For many years, gastrectomy has been performed under laparotomy. Since Kitano et al. (8) reported the first case of laparoscopy-assisted distal gastrectomy (LADG) for gastric

cancer in 1994, LADG has been widely performed in community hospitals not only for early disease but also for advanced tumors. Laparoscopic surgery provides a good quality of life in addition to cosmetic benefits. LADG is often selected when the tumors are located in the middle to the lower third of the stomach. Unlike LADG, total gastrectomy remains challenging under the laparoscopic approach and the technique has not been standardized.

The feasibility and safety of LADG was confirmed for T1 and T2N0 disease in Japanese Phase II (9) and Korean Phase III (KLASS trial, NCT00452751) trials (10). The non-inferiority of long-term survival will be confirmed in Japanese (JCOG-0912 trial, UMIN000003319) and Korean Phase III trials. Moreover, a Phase II/III trial is ongoing for advanced gastric cancer in Japan (JLSSG0901 trial, UMIN000003420). The Phase II part of this trial was finished, and the feasibility and safety of LADG was confirmed for advanced disease.

Thus, candidates for future standard treatment are multimodality treatments including neoadjuvant chemotherapy and LADG, when advanced tumors are located in the middle to the lower third of the stomach. However, LADG after neoadjuvant chemotherapy has not been evaluated in Phase II trials, although it has been presented to be safe and feasible in some Japanese medical meetings repeatedly (11).

Based on these, we conducted a randomized Phase II trial to compare LADG and open distal gastrectomy (ODG) after neoadjuvant chemotherapy for gastric cancer.

PROTOCOL DIGEST OF THE STUDY

Purpose

The purpose of the study is to evaluate the safety and efficacy of LADG compared with ODG for gastric cancer which is macroscopically resectable by D2 gastrectomy, to determine whether LADG can be a test arm for a future Phase III trial to evaluate the non-inferiority of overall survival compared with ODG in patients who receive neoadjuvant chemotherapy. To minimize the variability of chemotherapy regimens, we restrict to the patients who are enrolled in the Phase II trial of neoadjuvant chemotherapy (COMPASS-D trial, UMIN000006378) (12).

Study Setting and Protocol Review

The study is an open-label, randomized Phase II clinical trial. The protocol has been approved by the Protocol Review Committee of Kanagawa Standard Anti-cancer Therapy Support System (KSATTS).

Resources

Research grants are from the KSATTS.

Endpoints

The primary endpoint is the 3-year progression-free survival (PFS) rate. The secondary endpoints are the overall survival, surgical morbidity and mortality, R0 resection rate, R0R1 resection rate, conversion rate, efficacy and safety in patients who complete the surgery, and efficacy and safety in each subset.

Eligibility Criteria for the First Enrollment

The tumors are staged according to the 14th edition of the Japanese Gastric Cancer Classification (13).

The inclusion criteria are as follows:

(i) Histologically proven adenocarcinoma of the stomach.
(ii) Clinical T4aN0-N3 disease, confirmed by upper gastrointestinal endoscopy or an upper gastrointestinal series, and abdominal computed tomography (CT) and laparoscopy. The T and N stages are determined by the method of Habermann et al. (14).
(iii) The gastric tumors are located in the middle to lower third of the stomach, are macroscopically resectable by distal gastrectomy with D2 lymph node dissection, and R0 or R1 resection can be achieved.
(iv) No bulky lymph node metastasis is detected by abdominal CT.
(v) No pleural effusion, no ascites exceeding the pelvis and no metastasis to the peritoneum, liver or other distant organs are confirmed by abdominal pelvic CT.
(vi) No clinically apparent distant metastasis.
(vii) Age ranging between 20 and 80 years.
(viii) ECOG performance status 0–1.
(ix) Sufficient oral intake.
(x) No previous treatment with chemotherapy or radiation therapy for any tumors.
(xi) No previous surgery for the present disease.
(xii) The patients were enrolled in the COMPASS-D Phase II trial comparing neoadjuvant chemotherapy with two and four courses of S-1 plus cisplatin (SC) or S-1 plus cisplatin and docetaxel (SCD) by a two-by-two factorial design for patients with macroscopically resectable serosa-positive gastric cancer, and receive neoadjuvant chemotherapy.
(xiii) Written informed consent.

The exclusion criteria are as follows:

(i) Past history of upper abdominal surgery.
(ii) Past history of surgery for the gastrointestinal tract.
(iii) Body mass index exceeding 30 kg/m^2.

Eligibility Criteria for the Second Enrollment

(i) Patients received two or four courses of SC or SCD defined by the COMPASS-D trial.
(ii) The gastric tumors are macroscopically resectable disease by distal gastrectomy with D2 lymph node

dissection. Resectability is evaluated by upper gastrointestinal endoscopy and CT 7–21 days after the date when the anti-cancer drugs were given.

(iii) No T4b disease.

(iv) No bulky lymph node metastasis.

(v) Sufficient organ function, as evaluated by laboratory tests 7 days or more after the date when the anti-cancer drugs were given. When patients are recovering from myelosuppression, the revised criteria are shown in parentheses.

White blood cell count $\geq 3000/mm^3$ ($2000/mm^3$)
Platelet count $\geq 10.0 \times 10^4/mm^3$ ($5.0 \times 104/mm^3$)
Aspartate aminotransferase ≤ 100 IU/l
Alanine aminotransferase ≤ 100 IU/l
Total bilirubin ≤ 2.0 mg/dl
Serum creatinine ≤ 1.5 mg/dl

(vi) No need for emergency surgery due to bleeding or perforation of the primary tumor.

(vii) No need for emergency surgery due to stenosis.

(viii) No mechanical obstruction.

Registration

The participating investigators are instructed to send the first eligibility criteria report to the Data Center at the non-profit organization KSATTS. Eligible patients are registered as first enrollment. After finishing neoadjuvant chemotherapy, investigators are instructed to send the second eligibility criteria report to the Data Center at the non-profit organization KSATTS. The eligible patients are registered as the second enrollment and then randomized to open or laparoscopic distal gastrectomy as described in the next section by a centralized dynamic method using the following factors: chemotherapy [two courses of SC/four courses of SC/two courses of SCD/four courses of SCD] and institution as balancing variables. Information regarding the necessary follow-up examinations is then sent from the Data Center. The accrual starts in October 2011 and is to continue for 3 years.

Treatment Methods

After the completion of the neoadjuvant chemotherapy or when the tumors progress during the treatment, patients proceed to surgery. The patients enrolled in this study receive open or laparoscopic distal gastrectomy.

Group A: ODG with D2 lymph node dissection
Group B: Laparoscopic distal gastrectomy with D2 lymph node dissection

In both groups, the intraperitoneal cavity is checked to see whether R0 or R1 surgery is possible by D2 distal gastrectomy. When R0/R1 surgery is impossible, the protocol treatment is stopped. After confirming the resectability, dissection is started.

For Group B, the number of trocars is limited to 5 or 6. Reduced port surgery is prohibited. The length of the skin incision is limited to ≤ 6 cm. When a longer skin incision is necessary, the case is regarded to require conversion to open surgery. The protocol prohibits laparoscopic total gastrectomy and laparoscopic extended surgeries such as lymphadenectomy exceeding D2 and combined resection of other organs. When these types of surgery are necessary to achieve an R0/R1 resection, the surgeon must convert to open surgery. The operators of laparoscopic surgery are limited to the surgeons whose skills for laparoscopic distal gastrectomy are qualified by Japan Society for Endoscopic Surgery.

More invasive surgeries such as pancreaticoduodenectomy or Appleby's surgery are prohibited. The protocol treatment is to be stopped if curative surgery is not performed. When R0/R1 surgery is achieved, S-1 of 80 mg/m^2 p.o. daily for 28 days, every 6 weeks, is initiated within 6 weeks after surgery, and was continued for 1 year. After the completion of the protocol treatment, no other treatment is permitted until recurrence is noted.

Study Design and Statistical Methods

The present study is a randomized Phase II trial to evaluate the efficacy and safety of LADG compared with ODG. This study is primarily designed to evaluate the 3-year DFS rate of LADG and to demonstrate that it is not inferior to that of ODG. LADG will be considered to be promising for a subsequent Phase III trial if the Bayesian posterior probability of 'the difference of the 3-year DFS rate is less than the non-inferiority margin of 8%' is at least 50% (15). For safety, the point estimate of treatment-related death (TRD) is expected to be $\leq 5\%$ in each group.

The planned sample size is 80, with 40 cases per arm. This sample size provides 76% chance of satisfying the above criteria, under the hypothesis that the expected 3-year disease-free survival rate in each arm is 50%.

The primary analysis in this study aims to estimate the 3-year DFS rate. The DFS curves are constructed as time-to-event plots by using the Kaplan–Meier method (14), and the 3-year DFS and its 95% confidence interval are estimated. The 3-year DFS is compared based on the normal approximation of the 3-year DFS rate (z-test). The overall survival is also analyzed in the same manner. The surgical morbidity and mortality, R0 resection rate, R0R1 resection rate and conversion rate are calculated as proportions with exact confidence intervals and compared with the Fisher's exact test.

Interim Analysis and Monitoring

The Data and Safety Monitoring Committee (DSMC) independently review the report of trial monitoring regarding the efficacy and safety data from the present study. Based on the monitoring, the DSMC can consider early termination of a treatment regimen when the TRD exceeds 5% (three patients) in each group during the enrollment. The protocol

compliance, safety, and on-schedule study progress are also monitored by the DSMC.

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Conflict of interest statement

None declared.

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Laparoscopic Transhiatal Resection for Siewert Type II Adenocarcinoma of the Esophagogastric Junction: Operative Technique and Initial Results

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Abstract: Laparoscopic distal gastrectomy has gained wide acceptance, and laparoscopic total gastrectomy (LTG) and laparoscopic proximal gastrectomy (LPG) are now also performed for gastric cancer. We extended these techniques to treat Siewert type II adenocarcinoma of the esophagogastric junction (AEG). Ten patients with clinical T1 AEG type II underwent laparoscopic transhiatal (LTH) resection combined with LTG reconstructed by Roux-en-Y (LTH + LTG: n = 2) or LPG reconstructed by jejunal interposition (LTH + LPG: n = 8). Intracorporeal esophagojejunostomy was performed using a circular stapler, of which the anvil head was introduced transabdominally or transorally. The median operation time was 243 minutes, and blood loss was 25.5 g. There were no intraoperative complications or conversion to open surgery. No anastomotic leak was observed, but 1 diaphragmatic herniation to the left thoracic cavity occurred postoperatively. The median length of the proximal margin was 14.5 mm. This operation is technically feasible and can be safely performed after adequate experience of LTG or LPG, though esophagojejunostomy in the mediastinum is technically demanding.

Key Words: adenocarcinoma of the esophagogastric junction, laparoscopic surgery, transhiatal approach

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The incidence of adenocarcinoma of the esophagogastric junction (AEG) is increasing worldwide. Siewert proposed an AEG classification system in 1996,[1] which is now widely used and accepted. This classification defines AEG according to the position of the center of the main tumor as type I, II, and III,[1,2] which is a useful distinction for aiding selection of the appropriate surgical approach. Complete tumor resection (R0) and adequate lymph node dissection are thought to be associated with good long-term prognosis for all types of AEG. The distributions of the 3 types of AEG are reported to differ between western and eastern countries,[3–7] and most AEGs in Asian countries are type II or III,[4–7] with oncological characteristics similar to those of gastric cancer. Most AEG type III tumors in Japan tend to be managed as proximal gastric cancer. The transthoracic approach is generally recommended for type I, whereas the abdomino-transhiatal route is considered to be the optimal surgical approach for type II and III tumors.[3,8] The laparoscopic transhiatal (LTH) approach may thus represent an alternative to open surgery for the treatment of such AEGs.

Laparoscopic gastrectomy with systemic lymphadenectomy is being performed with increasing frequency, especially in Japan and Korea, which have high incidences of gastric cancer. Acceptable oncological outcomes and faster patient recovery times have been reported after laparoscopic surgery for early gastric cancer.[9] Laparoscopic distal gastrectomy is the most frequently performed procedure for lesions of the distal stomach, whereas laparoscopic total gastrectomy (LTG) and laparoscopic proximal gastrectomy (LPG) are also now being performed to treat cancer of the proximal stomach[10]; however, esophagojejunal anastomosis under laparoscopy remains a challenging procedure, preventing the widespread use of these procedures. We have the experience of many cases of LTG and LPG, and have extended the use of these techniques to treat AEG type II, which arises at the anatomic cardia. To date, few studies have reported the safety and feasibility of such procedures. In this study, we report the technical details and our preliminary experiences of LTH procedures for localized AEG type II.

PATIENTS AND METHODS

This preliminary technical report represents a single surgeon's experience (T.K.) at 2 institutions.

Patients

Ten patients (5 males, 5 females) with AEG type II underwent laparoscopic radical surgery between May 2009 and August 2011. The operative procedures in these patients included LTH distal esophagectomy combined with reconstruction by Roux-en-Y (LTH + LTG), or combined with LPG reconstructed by jejunal interposition (LTH + LPG). Preoperative staging was based on gastrointestinal endoscopy, endoscopic ultrasonography, barium swallowing, and computed tomography. The diagnosis in all patients was AEG type II, clinical stage T1N0, beyond the indication range for endoscopic mucosal resection or endoscopic submucosal dissection. The length of esophageal invasion from the esophagogastric junction was estimated to be <3 cm in all cases. Surgery was performed after the informed consent was obtained from the patients.

Surgical Procedures

The patient was placed in the supine position with legs spread. A camera port was placed at the umbilicus, through which a flexible endoscope with a 10-mm tip (Olympus Optical Ltd, Tokyo, Japan) was introduced. Four other

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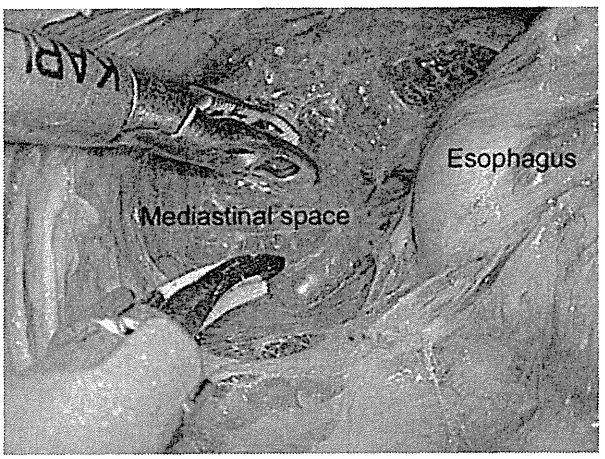

FIGURE 1. Transhiatal dissection of the distal esophagus in the mediastinum.

operating ports were created in the upper abdomen. The left lobe of the liver was retracted using a Penrose drain, as described by Sakaguchi et al.[11] Mobilization of the stomach and perigastric lymphadenectomy were initially performed, depending on the selected operative procedure. The perigastric lymph nodes and lymph nodes around the celiac trunk were removed (around the left gastric artery, common hepatic artery, and proximal side of the splenic artery). The left gastric artery was clipped and divided at the level of its root. Additional splenectomy was not performed. The phrenoesophageal membrane was subsequently divided to expose the abdominal esophagus circumferentially, and the distal esophagus in the mediastinum was then dissected upward from the hiatus and fully mobilized to obtain a sufficient proximal margin from the tumor (Fig. 1). The abdominal esophagus was encircled using cotton tape, which was pulled to stretch the esophageal wall. An anterior incision was sometimes made to the diaphragmatic crus using an ultrasonic coagulating device to widen the esophageal hiatus to improve the view in the mediastinal space. Only the periesophageal lymph nodes were dissected, and the extended mediastinal lymph nodes were not dissected. Intraoperative peroral endoscopy was carried out to determine the transection line of the esophagus. The esophagus was transected using an articulating endoscopic linear stapler (Echelon Flex, Ethicon Endosurgery, Cincinnati, OH) (Fig. 2).

In LTH + LTG, the umbilical port was extended vertically up to 3.5 cm and was protected and retracted using a wound retractor (Alexis Wound Retractor S; Applied Medical, Rancho Santa Margarita, CA). The entire stomach with the distal esophagus was removed through the incision. A 40-cm long Roux limb was then created intracorporeally for subsequent esophagojejunostomy. Jejunojejunal anastomosis (Y anastomosis) was performed using an endoscopic linear stapler (side-to-side).

In LTH + LPG, the left upper port (subcostal) was extended transversely up to 5 cm, through which the proximal stomach with distal esophagus was resected with a linear stapler at the upper third line. A 15-cm-long straight pedicled jejunum was then created for interposition through the mini-laparotomy. Jejunojejunal anastomosis was performed by handsewing under direct vision.

In all the cases, rapid pathologic examination of frozen sections was performed to assess the proximal surgical margins. After reestablishment of pneumoperitoneum, a 25-mm circular stapler anvil head was placed at the stump of the esophagus. In the initial 4 cases, the anvil head was placed by a transabdominal procedure using handsewn purse-string sutures, as described previously.[12] In these cases, a detachable bowel clamp (Endo intestinal clip; Aesculap, Tuttlingen, Germany) was placed at the esophagus proximally as far as possible, avoiding withdrawal of the esophagus into the mediastinum during purse-string suturing. In addition, a monofilament pretied loop was applied to ensure ligation. In the last 6 cases, a transoral delivery system using a pretilted anvil head (Orvil; Covidien, Norwalk, CT) was used, as described for usual LTG or LPG.[13,14] The Roux limb or pedicled jejunum was positioned in retrocolic manner to reduce tension to the anastomosis. Intracorporeal end-to-side esophagojejunostomy was performed using a circular stapler (Fig. 3), the main body of which was introduced through a surgical glove attached to the wound retractor at the mini-laparotomy. The distal stump of the jejunum was closed using a 60-mm endoscopic linear stapler. In LTH + LPG, jejunogastric anastomosis was performed using the 60-mm endoscopic linear stapler at the anterior wall of the gastric remnant in side-to-side manner (Fig. 4). Neither myotomy nor pyloroplasty was performed in the pyloric ring.

RESULTS

To date, 10 patients have successfully undergone LTH resection for AEG type II (2 LTH + LTG and 8 LTH + LPG). Two patients underwent LTH + LTG because they

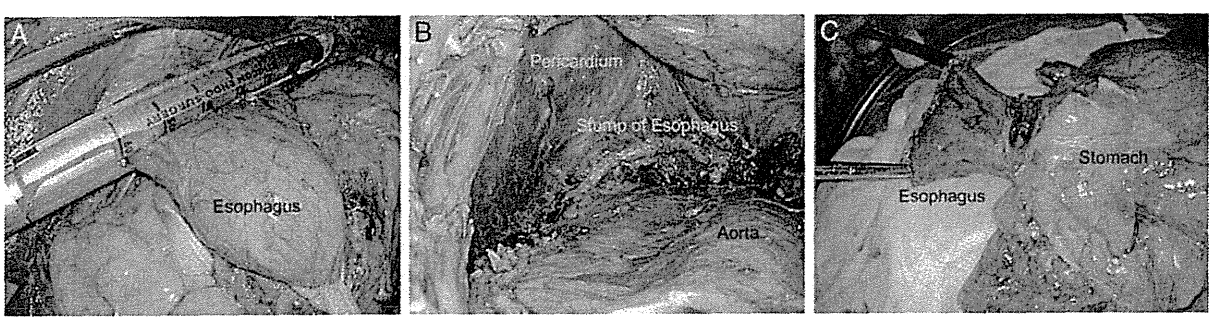

FIGURE 2. A, Transection of the distal esophagus using an articulating linear stapler. B, Mediastinal view after transection of the esophagus. C, Extracted specimen of the proximal stomach with the distal esophagus.

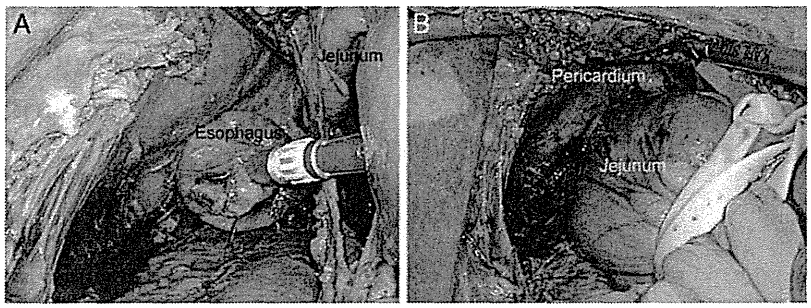

FIGURE 3. A and B, Intracorporeal esophagojejunal anastomosis using a circular stapler.

had synchronous early gastric cancer in the lower stomach. The median age of the patients was 64.1 years (range, 37 to 82 y) and the median body mass index was 23 (range, 18 to 26). The median operation time was 243 minutes (range, 186 to 321 min), the median estimated blood loss was 25.5 g (range, 3 to 108 g), and no transfusions were required. The times of requiring analgesia, in addition to the basal anesthesia, was 1.0 (range, 0 to 2). The median number of retrieved lymph nodes was 22.2 (range, 13 to 35). There were no severe intraoperative complications, and no conversion to open surgery was required in any patient. No postoperative anastomotic leaks or anastomotic stenosis were observed. A diaphragmatic hernia occurred on postoperative day 1 in one LTH + LPG patient, and emergency relaparoscopy was performed the same day. In this case, the omentum, transverse colon, and small intestine migrated to the left thoracic cavity through the enlarged esophageal hiatus. These organs were removed from the abdominal cavity laparoscopically and the enlarged hiatus was then repaired. In another LTH + LPG patient, postoperative gastric stasis developed, with a complaint of gastric fullness; this symptom was improved by conservative treatment, but the patient required a prolonged hospital stay (55 days). The other 9 patients recovered normal activity soon after the surgery, with a median postoperative hospital stay of 13 days (range, 9 to 20 d). They were allowed to take clear liquids on postoperative day 3 and solid food on day 4.

Pathologic findings revealed a median proximal resection margin of 14.5 mm (range, 10 to 23 mm) and a median circumferential margin of 3.6 mm (range, 2.4 to 4.5 mm). The median size of the tumor (maximum diameter) was 25.4 mm (range, 12 to 49 mm) and the median length of esophageal invasion was 18.6 mm (range, 2.5 to 20.0 mm). All the resections were R0, based on the final pathology reports.

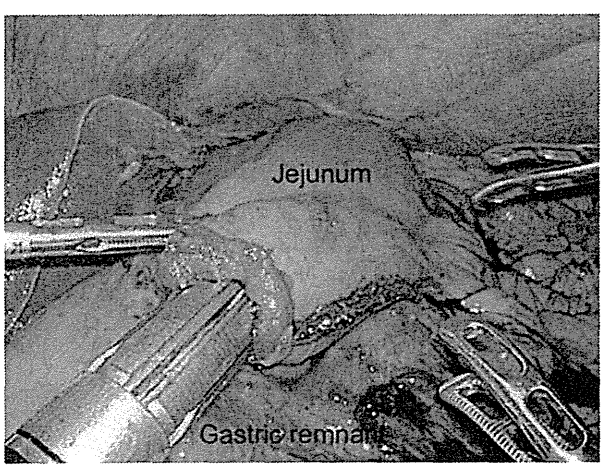

FIGURE 4. Intracorporeal jejunogastric anastomosis using a linear stapler in LTH+LPG. LPG indicates laparoscopic proximal gastrectomy; LTH, laparoscopic transhiatal resection.

DISCUSSION

Some clinical trials have suggested that a transhiatal approach by laparotomy is preferable to thoracotomy for AEG type II. The Japan Clinical Oncology Group (JCOG9502) demonstrated the superiority of the transhiatal approach over left thoracotomy for the treatment of AEG type II and III tumors. This approach was associated with lower morbidity when the length of esophageal invasion was < 3 cm.[8] In this context, we hypothesized that the laparoscopic technique could represent an alternative technique for treating AEG type II; and as for gastric cancer, when the tumor was in early stage and the esophageal invasion was ≤ 3 cm. We started to perform this procedure after the experience of 150 cases of laparoscopic distal gastrectomy and 40 cases of LTG or LPG for gastric cancer.

The concept of LTH esophagectomy was first reported by DePaula et al in 1995[15] and by Swanstrom and Hansen in 1997,[16] and similar operation using the inversion technique have been also reported by other researchers.[17] Montenovo et al[18] reported excellent outcomes of laparoscopic-assisted transhiatal esophagectomy for AEG. However, in all of these reports, reconstruction was performed by cervical anastomosis using the gastric tube. In contrast, reports of LTH resection for AEG with esophagojejunal anastomosis are lacking, probably due to the difficulties associated with anastomotic techniques. Only Patriti et al[19] has reported the preliminary outcomes of robot-assisted LTH resection in 17 patients with cardia cancer, including 3 cases of AEG type II.

From a technical point of view, enhanced laparoscopic visualization of the mediastinal space through the hiatus was thought to be preferable to open surgery, possibly reducing the risk of hemorrhage or complications. Indeed, our experiences suggest that meticulous dissection under a bloodless field could be performed using an ultrasonic coagulating device. In contrast, laparoscopic esophagojejunal anastomosis in the mediastinum is thought to be the most

difficult aspect of this operation. Advances in circular stapling devices have enabled surgeons to safely perform mediastinal anastomosis without using the thoracic approach, but esophagojejunostomy is still thought to be a challenging laparoscopic surgical technique, even in cases of usual LTG or LPG. For usual LTG or LPG, we used handsewn purse-string sutures to place the anvil head at the esophageal end, using detachable intestinal clips.[12] The same method was attempted in the initial 4 cases in this study, but this procedure at the higher esophagus was technically demanding, even when the hiatus was widened. From the fifth case, we therefore switched to transoral placement of the anvil head. This device was originally developed specifically for bariatric surgery, and allows the esophagus to be transected further proximally than before; furthermore, placement of the anvil head in the mediastinum becomes much easier to perform. However, the possible risk of injuring the esophageal wall during transoral delivery represents a potential drawback of this method. In addition, the long-term outcomes of the double-stapling esophagojejunal anastomosis, such as the incidences of leakage or stenosis, have not yet been established. Although sufficient clinical data for this device are lacking, we believe that it presents the most suitable option for higher anastomosis in the mediastinum.

Regarding the postoperative complications of esophagojejunostomy, anastomotic leak with mediastinitis is considered to be the most important and potentially life-threatening one; however, no instances of anastomotic leak occurred in the present series. We believe it is essential to secure the anastomoses to allow sufficient visibility, with adequate widening of the diaphragmatic crus. One diaphragmatic herniation (in the sixth case) occurred as a result of this enlargement. This complication has been also reported in esophagectomy with gastric tube replacement.[20] The enlarged diaphragmatic crus was meticulously repaired by suturing to prevent this complication in subsequent cases in the present series.

The oncological suitability of the laparoscopic procedure for treating AEG type II also needs to be evaluated. A safe proximal margin would minimize the anastomotic recurrence rate.[21] In our series, the adequate transection point was confirmed by intraoperative endoscopy, and the pathologic findings indicated that safe surgical margins as for T1 tumors were obtained in all patients. Several studies have also emphasized the importance of the circumferential margin as a prognostic factor in the surgical treatment of AEG,[22] and the distance of the circumferential margin was also satisfactory in our series. The median number of regional lymph nodes retrieved was 22.9, which was also satisfactory. The lymphatic spread of AEG was clearly demonstrated in a large-scale study by Siewert et al,[3] who reported lymphatic involvement of type II tumors mainly in the left (67%) and right (63%) paracardial regions, lesser curvature (66%), and toward the branch of the celiac trunk (25%). The reported occurrence of lower mediastinal lymph node metastasis from type II is 12%, but the incidence in T1 tumors is reported to be very low.[23] The range of lymph node metastases in the present series was similar to those in usual LTG or LPG for gastric cancer.

Regarding the quality of life, the cosmetic results were excellent after our procedure. All the patients recovered quickly and postoperative analgesia was minimized. No pulmonary-associated complications were recorded, probably due to the minimal damage to the body wall. In addition, gastric reservoir function was preserved in 8 patients who underwent LPG. Such function-preserving surgery through minimal access may further contribute to the patient quality of life.

Our preliminary experiences suggest that advances in instrumentation mean that LTH resection of localized AEG type II is technically feasible and can be performed safely after adequate experience of performing LTG or LPG for gastric cancer. However, it remains a complex, advanced laparoscopic procedure, with esophagojejunal anastomosis in the mediastinum being especially technically demanding. This procedure should presently only be performed by experienced laparoscopic surgeons. More cases need to be examined and future, prospective clinical trials may be needed to assess the benefits of these surgical techniques.

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Laparoscopic proximal gastrectomy with jejunal interposition for gastric cancer in the proximal third of the stomach: a retrospective comparison with open surgery

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Abstract
Background The incidence of cancer in the proximal third of the stomach is increasing. Laparoscopic proximal gastrectomy (LPG) seems an attractive option for the treatment of early-stage proximal gastric cancer but has not gained wide acceptance because of technical difficulties, including the prevention of severe reflux. In this study, we describe our technique for LPG with jejunal interposition (LPG-IP) and evaluate its safety and feasibility.
Methods In this retrospective analysis, we reviewed the data of patients with proximal gastric cancer who underwent LPG-IP ($n = 22$) or the same procedure with open surgery (OPG-IP; $n = 68$) between January 2008 and September 2011. Short-term surgical variables and outcomes were compared between the groups. The reconstruction method was the same in both groups, with creation of a 15 cm, single-loop, jejunal interposition for anastomosis.
Results There were no differences in patient or tumor characteristics between the groups. Operation time was longer in the LGP-IP group (233 vs. 201 min, $p = 0.0002$) and estimated blood loss was significantly less (20 vs. 242 g, $p < 0.0001$). The average number of harvested lymph nodes did not differ between the two groups (17 vs. 20). There also were no differences in the incidence of leakage at the esophagojejunostomy anastomosis (9.1 vs. 7.4 %) or other postoperative complications (27 vs. 32 %). The number of times additional postoperative analgesia was required was significantly less in the LPG-IP group compared with the OPG-IP group (2 vs. 4, $p < 0.0001$).
Conclusions LPG-IP has equivalent safety and curability compared with OPG-IP. Our results imply that LPG-IP may lead to faster recovery, better cosmesis, and improved quality of life in the short-term compared with OPG-IP. Because of the limitations of retrospective analysis, a further study should be conducted to obtain definitive conclusions.

Keywords Proximal gastrectomy · Laparoscopic surgery · Jejunal interposition · Gastric cancer

The safety and efficacy of laparoscopic gastrectomy for the treatment of early gastric cancer have been demonstrated in many clinical studies [1–3]. An increasing number of laparoscopic gastrectomies are currently being performed, especially in eastern countries, which have high incidences of gastric cancer. Because gastric cancer has predominantly been located in the distal stomach in eastern countries, laparoscopic distal gastrectomy for cancer in the middle and distal stomach has been the more commonly performed surgical procedure. However, Japanese surgeons are confronted with an increasing number of gastric cancers involving the proximal third of the stomach, probably because of the aging population. For advanced cancer in the proximal third of the stomach, total gastrectomy with D2 lymph node dissection is standard in Japan [4]. For early-stage cancer in the proximal third, open proximal gastrectomy has been performed to preserve physiological function of the remaining stomach [5–7]. Early cancer is estimated to account for nearly 50 % of gastric cancer currently diagnosed in Japan [8]. In this context,

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