Surg Endosc (2013) 27:2877–2885
DOI 10.1007/s00464-013-2848-0

Morbidity and mortality after laparoscopic gastrectomy for advanced gastric cancer: results of a phase II clinical trial

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Received: 11 November 2012 / Accepted: 16 January 2013 / Published online: 13 February 2013

Abstract
Background Very few reports are available on laparoscopic gastrectomy (LG) for advanced gastric cancer (AGC) patients. We therefore conducted a prospective phase II clinical trial to address the feasibility of LG in AGC. Morbidity and mortality were evaluated.
Methods The eligibility criteria were as follows: 20–80 years of age, cT2N0–cT4aN2, American Society of Anesthesiologists score of 3 or less, and no other malignancy. A total of 204 patients were enrolled onto this study. Of these, 16 were excluded because far-advanced stages of disease were identified after laparoscopic exploration, and 31 were excluded because early gastric cancer was diagnosed postoperatively. All patients underwent a D2 lymphadenectomy. Morbidity was stratified according to the Clavien–Dindo classification.
Results Conversion to open surgery occurred in 11 patients (7.0 %). The mean hospital stay was 6.3 days for distal gastrectomy and 8.5 days for total gastrectomy. The mean number of collected lymph nodes was 52.7 for distal gastrectomy and 63.8 for total gastrectomy. The rates of local and systemic complications of grade II or more were 8.3 and 3.2 %. One patient died of operative complications. In multivariate analysis, old age (>70 years) was an independent risk factor for complications, and old age and Billroth I anastomosis were predictable risk factors for local complications.
Conclusions LG with D2 lymphadenectomy was safe and technically feasible for the treatment of AGC, with acceptable rate of morbidity and mortality. ClinicalTrial.gov Registration: NCT01441336.

Keywords Advanced gastric cancer · Laparoscopic gastrectomy · Morbidity · Short-term outcomes

Laparoscopic gastrectomy (LG) for the treatment of early gastric cancer (EGC) has gained acceptance as it is a minimally invasive procedure and is now regarded as a suitable alternative to open surgery for the management of EGC. Many studies have reported early results and conclude that LG for EGC is safe and provides several benefits, such as a shorter hospitalization, earlier mobilization, earlier functional recovery, and comparable complication rates with open surgery [1–5]. However, the oncological safety of using LG for the treatment of EGC is still controversial. Two randomized controlled trials to compare long-term survival after LG and open gastrectomy (OG) for EGC are currently ongoing in Japan and Korea (JCOG 0912 and KLASS 01 trials), and the results are awaited [6].

With the accumulation of experience, use of LG has been broadened to patients with advanced gastric cancer (AGC). Recently, many retrospective comparative studies have reported that LG for AGC was safe and feasible when compared to the short-term and long-term outcomes observed with OG [7–9]. However, most retrospective studies did not include a satisfactory number of patients to establish clinical evidence and included the majority of clinical EGC patients preoperatively diagnosed. Moreover, there was no prospective study when we started this study.

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Therefore, we conducted this prospective phase II trial (single arm study) to evaluate the feasibility of LG for AGC. We reported operative morbidity and mortality data, one of the secondary end points of this trial. The analysis of disease-free survival (primary end point) is scheduled to take place in 2015.

Materials and methods

Patients

This clinical study was initiated in November 2008. The primary end point was 3 year disease-free survival, and the secondary end points were morbidity and mortality, 3, 5, and 7 year overall survival, and recurrence pattern. The eligibility criteria were as follows: a histologically confirmed adenocarcinoma of the stomach; cT2N0M0–cT4aN3M0 (American Joint Committee on Cancer/Union Internationale Contre le Cancer 7th edition); 20–80 years of age; a score of 3 or less according to the American Society of Anesthesiologists; and no other malignancy. Exclusion criteria were as follows: far advanced stages of cancer such as adjacent organ invasion or peritoneal seeding identified by laparoscopic exploration, and EGC diagnosed postoperatively. Endoscopic ultrasonography and stomach computed tomography were performed routinely for preoperative staging. When the clinical stages between the two diagnostic methods differed, higher stage was adopted. The study was approved by the institutional review board of the Seoul National University Bundang Hospital, and all patients provided written informed consent.

Surgical techniques

All surgeries were performed by a single surgeon (H-HK). The type of gastric resection was determined according to tumor location. Distal gastrectomy (DG) was indicated for lesions in lower third and/or low body of the stomach. Total gastrectomy (TG) was indicated for lesions located above the mid body of the stomach.

A pneumoperitoneum was established by the open technique, and six trocars were used. A 10 mm version flexible videoscope (EndoEye camera system, Olympus Medial Systems Corp., Tokyo, Japan) and a Harmonic scalpel (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) were used to facilitate dissection. A D2 lymph node dissection was performed in all patients (Fig. 1). Total omentectomy was performed for tumors with serosa exposure identified by laparoscopic exploration. After full mobilization of the stomach, a 4–5 cm transverse incision in epigastrium was made for removal of the specimen and reconstruction during DG. When the tumor was located in the lower third of the stomach, the Billroth I (BI) method was used, but if the tumor extended to the upper part of the stomach, was close to the pylorus, then uncut Roux-en-Y or Billroth II (BII) with Braun anastomosis was used. If long-term survival was expected (age <70 years or relatively low-stage disease), uncut Roux-en-Y anastomosis was more preferred than BII with Braun anastomosis to prevent bile reflux. Uncut Roux-en-Y reconstruction was performed in the manner (stapling using a linear cutter without a knife across the afferent jejunal limb after BII with Braun reconstruction) described by Uyama et al. [10]. Intracorporeal end to side Roux-en-Y reconstruction using a circular stapler and an endoscopic purse string instrument (Endo-PSI(II), Chiba, Japan, or Lap-Jack, Eterne, Gyeong-gi, Korea) was performed after TG, as we have reported previously [11]. During TG, concomitant splenectomy was performed to ensure complete dissection of the no. 10 lymph nodes when the tumor was located in upper third, revealing serosa exposure under laparoscopic exploration, or when no. 10 lymph node metastasis was suspected before surgery.

Postoperative care

A standard clinical pathway was applied to all patients. A nasogastric tube was not inserted. One or two surgical drains were routinely inserted and removed after a liquid diet could be tolerated. Sips of water were permitted 2 days after DG and 3 days after TG; a liquid diet was started 3 days after DG and 4 days after TG; and a semisolid diet was started if the patient was able to tolerate three liquid diet meals. The patients were discharged 5 days after DG and 6–7 days after TG if they could tolerate more than three semisolid diet meals. During the preoperative, intraoperative, and postoperative periods, all patients were observed and data recorded.

Definition of complication

Adverse events were defined as complications that occurred within 30 days of surgery. When complications occurred in association with surgical technique near the operation field, such as wound or intra-abdominal cavity, they were considered local complications. A complication was classified as systemic when the complication was not associated with the operation field [12]. They were also classified according to a grading system suggested by Dindo et al. [13]. Grade I was any deviation from the normal postoperative course allowing symptomatic therapeutics such as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. Grade II included pharmacological treatment with drugs other than those allowed for grade I complications (antibiotics, parenteral

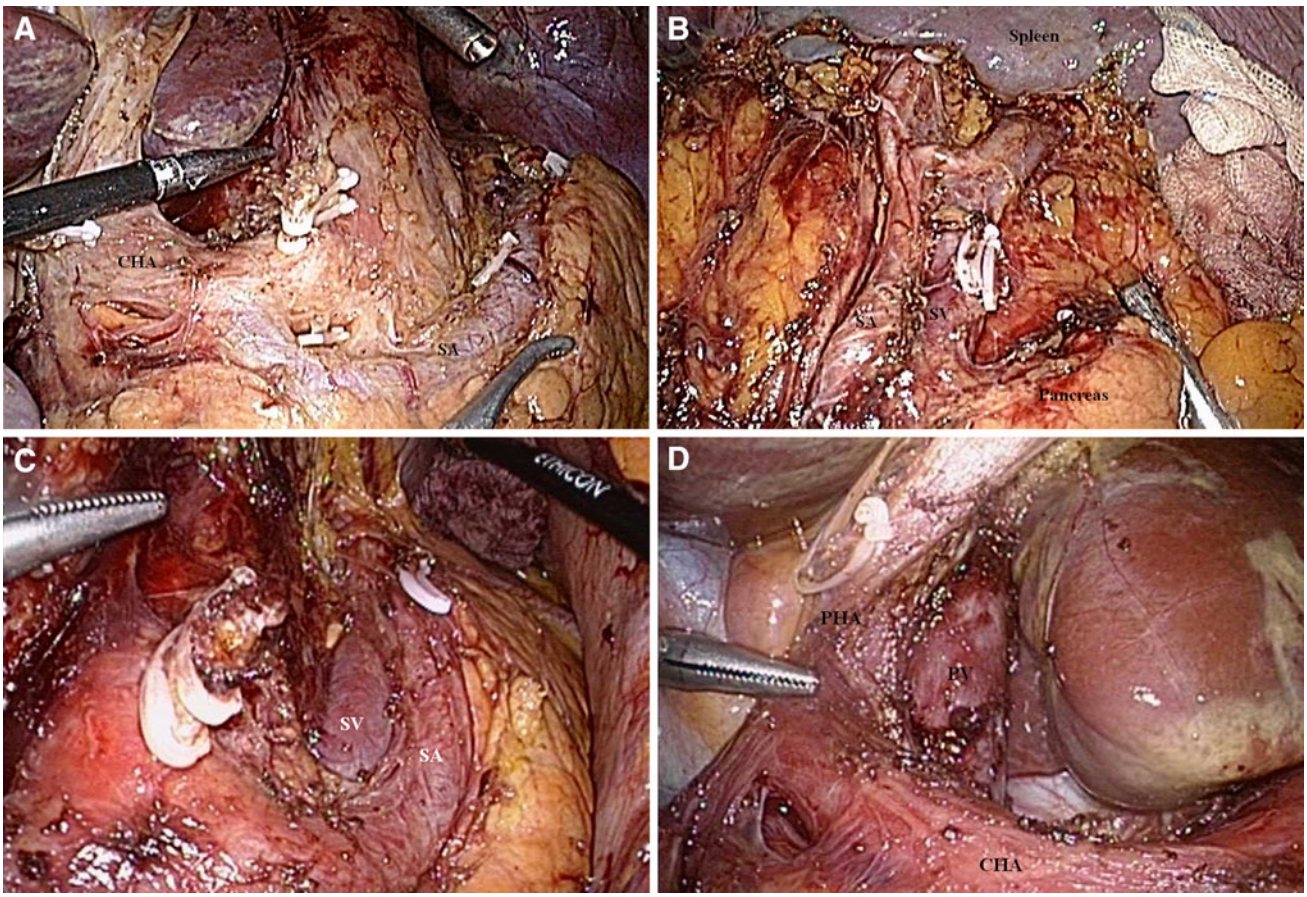

Fig. 1 D2 lymphadenectomy. **A** Suprapancreatic dissection. **B** Spleen and distal pancreas preserving lymph node 10 and 11d station dissection. **C** Lymph node 11p station dissection. Splenic vein was exposed to ensure the complete dissection if possible. **D** Lymph node 12a station dissection. Along proper hepatic artery, lymph node 12a station was dissected and portal vein was always exposed to ensure the complete dissection. *SA* splenic artery, *SV* splenic vein, *CHA* common hepatic artery, *PHA* proper hepatic artery, *PV* portal vein

nutrition, and blood transfusions). Grade III were postoperative complications requiring surgical, endoscopic, or radiologic intervention with (grade IIIb) or without general anesthesia (grade IIIa). Grade IV included life-threatening complications requiring intensive care unit management. Grade V was defined by postoperative death of the patient. When more than one complication occurred in a patient, only the most severe complication was taken into account.

Sample size and statistical analysis

The results of a previous multicenter study on the long-term outcomes after curative OG plus adjuvant chemotherapy in AGC served as the basis for determining the required numbers of patients in our study [14]. According to the study, the expected 3 year recurrence-free survival rate is 70 % in AGC patients. The sample size was 143, provided 80 % power under the hypothesis of primary end point as the expected value of 70 % and threshold value of 60 % using one-sided testing at a 5 % significance level. Allowing for a 10 % dropout rate, the sample size was calculated to be 157.

Descriptive data were presented as mean ± standard deviation. The χ^2 test was used for comparisons between two groups. Multivariate analysis was performed by a binary logistic regression model. All the statistical analyses were performed by SPSS software, version 18.0 (SPSS Inc., Chicago, IL, USA). A p value of ≤ 0.05 was considered statistically significant.

This study was registered with ClinicalTrial.gov (http://clinicaltrials.gov/), identification number NCT01441336.

Results

Patient characteristics

A total of 204 patients were enrolled from November 2008 to June 2012. Of these, 16 were excluded because

laparoscopic exploration revealed that the cancer was too advanced (adjacent organ invasion in nine cases, peritoneal seeding in four cases, conglomerated lymph node metastasis in two cases, and para-aortic lymph node metastasis in one case). Preoperatively diagnosed cT3N0 ($n = 3$), cT3N1 ($n = 3$), cT3N2 ($n = 1$), cT4aN0 ($n = 2$), cT4aN1 ($n = 3$), cT4aN2 ($n = 2$), and cT4aN3 ($n = 2$) disease were associated with this exclusion criteria. Adjacent organ invasion included the pancreas in three patients, the transverse colon in two patients, the mesocolon in three patients, and the diaphragm crus in one patient. Among these patients, curative resection was possible in six patients, laparotomy in four patients (two combined mesocolon resections, one transverse colon resection, and one distal pancreatectomy) and laparoscopically in two patients (one combined mesocolon resection and one distal pancreatectomy). Thirty-one patients diagnosed with EGC postoperatively were also excluded. Preoperative stages related to those patients were cT2N0 ($n = 13$), cT2N1 ($n = 4$), cT3N0 ($n = 8$), cT3N1 ($n = 4$), cT3N2 ($n = 1$), and cT4aN0 ($n = 1$). Preoperative diagnosis accuracy was 76.9 % (157 of 204).

Patient characteristics are summarized in Table 1. Out of the 157 patients included in this series, 105 were men and 52 were women, with a mean age of 60.89 ± 12.39 (range, 22–80) years and a mean body mass index of 23.72 ± 2.83 kg/m^2. DG was performed on 115 patients and TG was performed on 42 patients. After DG, BI reconstruction was performed in 35 patients, BII with Braun anastomosis in eight, and uncut Roux-en-Y in 72. Seven patients had a microscopic positive resection margin (R1 resection, positive proximal resection margin in four patients and distal margin in three patients). From the intraoperative findings, serosa exposure or extended lymph node metastasis was suspected in these cases. Therefore, no procedures such as thoracotomy or pancreaticoduodenectomy were performed to achieve R0 resection, as is the policy with open surgery in our center. Complete resection (R0) was achieved in the remaining 150 patients. Combined splenectomy was performed in 23 patients. Ten patients underwent combined other organ resections, seven cholecystectomies for gallbladder stones or polyps, two left adrenalectomies for incidentalomas, and one appendectomy for chronic appendicitis. Total omentectomy was performed in 39 patients and partial omentectomy in 118 patients. The tumor depths were as follows: T2, 45 (28.7 %); T3, 57 (36.3 %); and T4a, 55 (35.0 %). The N stages were as follows: N0, 48 (30.6 %); N1, 24 (15.3 %); N2, 27 (17.2 %); N3a, 28 (17.8 %); and N3b, 30 (19.1 %). Tumor stages were: stage IB, 25 (15.7 %); stage IIA, 28 (17.8 %); stage IIB, 17 (10.8 %); stage IIIA, 25 (15.9 %); stage IIIB, 28 (17.8 %); and stage IIIC, 34 (21.7 %).

Table 1 Clinicopathologic characteristics of 157 patients

Characteristic	Value
Age, years, mean ± SD	60.89 ± 12.39
Sex, M:F	105:52
Body mass index, kg/m^2, mean ± SD	23.72 ± 2.83
Type of operation	
Distal gastrectomy	115 (73.2 %)
Total gastrectomy	42 (26.8 %)
Type of reconstruction	
Billroth I	35 (22.3 %)
Billroth II with Braun anastomosis	8 (5.1 %)
Uncut Roux-en-Y	72 (45.9 %)
Roux-en-Y	42 (26.8 %)
ASA score	
1	75 (47.8 %)
2	72 (45.9 %)
3	10 (6.4 %)
Combined splenectomy	
No	134 (85.4 %)
Yes	23 (14.6 %)
Combined other operation	
No	147 (93.6 %)
Yes	10 (6.4 %)
Omentectomy	
Total	39 (24.8 %)
Partial	118 (75.2 %)
Radicality	
R0	150 (95.5 %)
R1	7 (4.5 %)
pT	
T2	45 (28.7 %)
T3	57 (36.3 %)
T4a	55 (35.0 %)
pN	
N0	48 (30.6 %)
N1	24 (15.3 %)
N2	27 (17.2 %)
N3a	28 (17.8 %)
N3b	30 (19.1 %)
pStage	
IB	25 (15.9 %)
IIA	28 (17.8 %)
IIB	17 (10.8 %)
IIIA	25 (15.9 %)
IIIB	28 (17.8 %)
IIIC	34 (21.7 %)

ASA American Society of Anesthesiologists

Surgical outcomes

The open conversion rate was 7.0 % (11 of 157). The most common reasons for open conversion were severe

adhesions secondary to previous upper abdominal surgery ($n = 4$), followed by uncontrollable bleeding due to spleen injury ($n = 2$) and bleeding tendency of unknown origin ($n = 1$). Other reasons included the possibility of inadequate node dissection due to obesity ($n = 1$), arrhythmia secondary to pneumoperitoneum ($n = 1$), injury to the splenic artery ($n = 1$), and splenic vein ($n = 1$).

The mean operating times for DG and TG were 191.7 ± 52.6 (range, 95–305) min and 236.1 ± 56.4 (range, 150–360) min, respectively. The mean postoperative hospital stay was 6.3 ± 2.3 (range, 5–18) days for DG and 8.5 ± 4.8 (range, 6–36) days for TG. The mean time to first soft diet uptake was 3.4 ± 1.3 days for DG and 4.3 ± 1.2 days for TG The mean number of collected lymph nodes was 52.7 ± 16.5 (range, 20–148) for DG and 63.8 ± 19.3 (range, 29–128) for TG. The mean blood loss was 136.2 ± 121.8 (range, 10–750) mL for DG and 160.9 ± 129.3 (range, 10–600) mL for TG. The open conversion rate was not different between patients undergoing DG and TG (8 of 115, 7.0 % vs. 3 of 42, 7.1 %; $p = 0.985$).

Postoperative complications according to the Clavien–Dindo classification

Tables 2 and 3 list the observed morbidities for all patients. Postoperative complications occurred in 56 patients (35.7 %), 41 (35.7 %) for DG and 15 (35.7 %) for TG. Systemic complications accounted for 25.5 % of all cases, 27.8 % (32 of 115) for DG and 19.0 % (8 of 42) for TG.

Table 2 Postoperative morbidity: systemic complications

Complication	LDG ($n = 115$)	LTG ($n = 42$)	Total ($n = 157$)
Grade I	27 (23.5 %)	8 (19.0 %)	35 (22.3 %)
Fever	10 (8.7 %)	5 (11.9 %)	15 (9.6 %)
Atelectasis or pleural effusion	9 (7.8 %)	3 (7.1 %)	12 (7.6 %)
Transient LFT abnormality	8 (7.0 %)	–	8 (5.1 %)
Grade II	3 (2.6 %)	0 (0 %)	3 (1.9 %)
Pneumonia	1 (0.9 %)	–	1 (0.6 %)
Atrial fibrillation	1 (0.9 %)	–	1 (0.6 %)
Urinary tract infection	1 (0.9 %)	–	1 (0.6 %)
Grade IIIa	1 (0.9 %)	0 (0 %)	1 (0.6 %)
Pleural effusion	1 (0.9 %)	–	1 (0.6 %)
Grade IVa	1 (0.9 %)	0 (0 %)	1 (0.6 %)
Pulmonary edema	1 (0.9 %)	–	1 (0.6 %)
Total complications	32 (27.8 %)	8 (19.0 %)	40 (25.5 %)

LDG laparoscopic distal gastrectomy, *LTG* laparoscopic total gastrectomy, *LFT* liver function test

Local complications accounted for 10.2 %, 7.8 % (9 of 115) for DG and 16.7 % (7 of 42) for TG. There were no significant differences in the incidences of local and systemic complications between DG and TG ($p = 0.264$ for systemic complication and $p = 0.135$ for local complication). The most frequent systemic complication was fever (9.6 %), followed by pulmonary problems (8.9 %; 12 grade I, one grade II, and one grade IIIa complications) and transient hyperbilirubinemia or/and elevated liver enzymes (5.1 %). The most frequent local complication was pancreatic fistula (3.2 %), which was treated with antibiotics in four patients (grade II) and observed in one patient (grade I). There were two anastomosis leakages after DG with BI anastomosis. One patient experienced anastomosis stricture after BI reconstruction, which was treated using endoscopic balloon dilatation.

No patient had to undergo reoperation as a result of postoperative complications. One patient died during hospitalization. The case of death was esophagus and remnant stomach infarction. The patient had chronic obstructive pulmonary disease, diastolic cardiomyopathy, and chronic renal insufficiency as comorbidities. He had undergone open conversion as a result of hypotension and atrial fibrillation after establishment of pneumoperitoneum.

Four patients were readmitted within 30 days of surgery because of grade IIIa postoperative complications. The

Table 3 Postoperative morbidity: local complications

Complication	LDG ($n = 115$)	LTG ($n = 42$)	Total
Grade I	2 (1.7)	1 (2.4)	3 (1.9)
Chylous drainage	1 (0.9)[a]	–	1 (0.6)
Wound	1 (0.9)[a]	–	1 (0.6)
Pancreas fistula	–	1 (2.4)	1 (0.6)
Paralytic ileus	1 (0.9)	–	1 (0.6)
Grade II	1 (0.9)	4 (9.5)	5 (3.2)
Pancreas fistula	1 (0.9)	3 (7.1)	4 (2.5)
Fluid collection	–	1 (2.4)	1 (0.6)
Grade IIIa	5 (4.3)	2 (4.8)	7 (4.5)
Fluid collection	1 (0.9)	–	1 (0.6)
Intra-abdominal abscess	–	2 (4.8)	2 (1.3)
Anastomosis leakage	2 (1.7)	–	2 (1.3)
Anastomosis stricture	1 (0.9)	–	1 (0.6)
Splenic artery pseudoaneurysm	1 (0.9)	–	1 (0.6)
Grade V	1 (0.9)	–	1 (0.6)
Esophagus and remnant stomach infarction	1 (0.9)	–	1 (0.6)
Total complications	9 (7.8)	7 (16.7)	16 (10.2)

LDG laparoscopic distal gastrectomy, *LTG* laparoscopic total gastrectomy

[a] One patient had two complications

causes of readmission were anastomotic leakage, anastomotic stricture, intra-abdominal abscess, and splenic artery pseudoaneurysm.

Risk factors related to morbidity

If grade I complications are excluded, the morbidity rate was 11.5 %. The risk factors associated with more than grade II complications were analyzed. Multivariate analysis revealed that age (>70 years) was an independent risk factor for the occurrence of complications (grade II or more) (Table 4). When factors associated with local complications (grade II or more) were analyzed, old age (>70 years) and anastomosis pattern (BI) were identified as independent risk factors associated with local complications according to the multivariate analysis (Table 5).

Among 11 patients who had experienced an open conversion event, complications developed in nine patients, and complications of grade II or more occurred in six. The reasons for open conversion related to complications (grade II or more) were uncontrollable bleeding ($n = 2$), obesity ($n = 1$), splenic artery injury ($n = 1$), severe adhesion ($n = 1$), and atrial fibrillation resulting from pneumoperitoneum ($n = 1$).

Table 4 Risk factors related to morbidity (grade II or higher)

Variable	Hazard ratio	95 % CI	*p*
Age			0.003
≤70 years	1		
>70 years	5.834	1.839–18.512	
Gender			0.933
Male	1		
Female	0.951	0.297–3.048	
Body mass index			0.783
<25 kg/m^2	1		
≥25 kg/m^2	0.846	0.257–2.782	
Comorbidity			0.116
None or 1	1		
≥2	2.543	0.793–8.151	
Type of operation			0.481
Distal	1		
Total	0.452	0.05–4.112	
Type of reconstruction			0.316[a]
Billroth II or uncut Roux-en-Y	1		
Billroth I	2.258	0.460–11.093	
Omentectomy			0.623
Partial	1		
Total	1.369	0.392–4.785	
Combined splenectomy or pancreatectomy			0.105
No	1		
Yes	7.181	0.66–78.119	
Combined operation			0.116
No	1		
Yes	2.543	0.793–8.151	
pT			0.425
T2–3	1		
T4a	1.652	0.481–5.671	
pN			0.973
N0	1		
N1–3	1.023	0.275–3.805	

CI confidence interval

[a] The *p* value was calculated from multivariate analysis in patients underwent distal gastrectomy only

Discussion

There have been several studies published on LG for AGC patients since 2008 [7–9, 15–19]. However, those were almost retrospective studies, and they were performed on a relatively small number of patients and only for a relatively short follow-up period. Furthermore, the majority of patients included in those studies were diagnosed with AGC postoperatively. Thus, we conducted this prospective study. We evaluated the morbidity and mortality of the patients who were enrolled onto this study. LG for the treatment of AGC could be performed safely with reasonable postoperative complication rates, and the laparoscopic proper D2 lymphadenectomy could be carried out with mean number of collected lymph nodes of 52.7 for DG and 61.5 for TG.

D2 lymphadenectomy has been considered a standard procedure for AGC in Japan and other Asian countries. Moreover, it was demonstrated by the long-term follow-up results of a randomized nationwide trial that D2 lymphadenectomy is associated with lower locoregional recurrence and gastric cancer–related death rates than D1 surgery [20]. Thus, the analysis of oncologic adequacy of LG for AGC by our final results will be valid because D2 lymphadenectomy was performed in all patients enrolled onto our study.

Less invasiveness of laparoscopic approach has been already demonstrated by many studies. Therefore, in the present study, we focused on the safety aspects of LG with D2 lymphadenectomy. Although all surgeries were performed by a very experienced surgeon, the open conversion rate was somewhat higher in the present study than in a previous study we did, and higher than in other studies that dealt mainly with patients with clinical EGC who underwent LG [2, 4, 5, 12]. Laparoscopic D2 lymphadenectomy seems to be a technically demanding procedure even when performed by surgeons with extensive experience of laparoscopic gastrectomies. The relatively high open conversion

Table 5 Risk factors related to local complication (grade II or higher)

Variable	Hazard ratio	95 % CI	*p*
Age			0.021
≤70 years	1		
>70 years	5.054	1.278–19.984	
Gender			0.838
Male	1		
Female	1.147	0.308–4.277	
Body mass index			0.633
<25 kg/m^2	1		
≥25 kg/m^2	1.37	0.376–4.979	
Comorbidity			0.355
None or 1	1		
≥2	1.913	0.483–7.575	
Type of operation			0.747
Distal	1		
Total	0.688	0.071–6.647	
Type of reconstruction			0.032[a]
Billroth II or uncut Roux-en-Y	1		
Billroth I	15.599	1.267–192.117	
Omentectomy			0.361
Partial	1		
Total	1.872	0.488–7.180	
Extended surgery			0.13
No	1		
Yes	6.251	0.583–66.987	
Combined operation			0.961
No	1		
Yes	0.943	0.091–9.738	
pT			0.124
T2–3	1		
T4a	3.104	0.734–13.125	
pN			0.781
N0	1		
N1–3	0.794	0.157–4.027	

CI confidence interval

[a] The *p* value was calculated from multivariate analysis in patients underwent distal gastrectomy only

rate was partly because consecutive AGC patients who met the eligibility criteria who visited the outpatient clinic were referred to us to participate in this study. In other words, the selection biases by surgeon were excluded, so the stages of the disease were well distributed. This will enable us to compare the long-term outcomes in the final analysis with those of previous reports on open surgery.

Using the Clavien–Dindo classification, the overall morbidity rate was 35.6 %. If grade I complications, which were mainly recognized as noncomplications, are excluded, the morbidity rate was 11.5 %. This figure is comparable to that of previous studies associated with conventional OG, which reported 14.0–24.5 % as the overall complication rate [21, 22]. However, in terms of minimal invasiveness, grade I complication rates have an important meaning. In this study, grade I complication rates after a laparoscopic DG (25.2 %) were similar to those observed for open DG (27.7 %) in our previous report, which compared and classified complications after laparoscopic assisted and open DG using the Clavien–Dindo classification [23]. Although we were unable to compare our findings directly, it seems that the laparoscopic approach of extended surgery is not less invasive. Those issues need to be discussed further in the context of the results of ongoing phase III trials.

The complication rates for laparoscopic TG are reported to be higher than those for laparoscopic DG because of technical difficulties [24, 25]. However, in the present study, the complication rates were not statistically different between both methods. Moreover, there was no complication related to esophagojejunostomy, which is regarded as one of the most common complications after laparoscopic TG [25]. The circular stapling technique in esophagojejunostomy anastomosis, which is used during conventional open TG, was applied to most patients undergoing laparoscopic TG in this study. The low anastomosis-related complication rate seems to be due to this stabilized technique performed by an experienced surgical team [26]. However, this study was limited by its small patient population and its lack of comparison with conventional open TG. A randomized controlled multicenter trial is needed to address whether this method can be applied universally.

According to the literature, old age is a significant risk factor for complications in gastric cancer surgery [21, 22]. However, a retrospective multicenter study performed in Korea reported that there were no significant differences in postoperative morbidity or mortality after laparoscopic subtotal gastrectomy between patients aged 45–69 years and those aged 70 years or more, although comorbidity was more common and postoperative hospital stay was longer in elderly patients [27]. Our previous data also demonstrated that complications after laparoscopic assisted distal gastrectomy (LADG) in gastric cancer patients >70 years of age were similar to those observed in younger patients [28]. In the present study, old age (>70 years) was an independent risk factor for complications. Extended surgery is still risky for elderly patients regardless of whether the approach is open or laparoscopic. Finding the optimal extent and approach after an appropriate assessment of the risks and benefits is particularly important in elderly patients.

In the present study, the anastomosis pattern was another significant risk factor for local complications The local

complication rate was higher in BI reconstruction than in BII or uncut Roux-en-Y reconstruction. Kojima et al. [29] reported that three patients (5 %) developed anastomotic leakage and four patients (6 %) experienced anastomotic stricture after LADG with BI anastomosis, whereas no anastomotic leakage and one (1 %) anastomotic stricture were encountered in the Roux-en-Y group. Fujiwara et al. [30] reported that the incidence of anastomotic leakage was 14 % (6 out of 43) in patients who underwent LADG with BI anastomosis. They believed that excessive duodenal stump devascularization and tension on the anastomosis could be causative factors for anastomosis-related complications. On the other hands, our previous retrospective study demonstrated that the anastomosis pattern after LADG in EGC patients was not an independent risk factor for complications [23].

In the present study, among 35 patients who underwent BI reconstruction, anastomosis-related complications were occurred in three patients. There was no anastomosis leakage or stricture in 80 patients who underwent BII with Braun anastomosis or uncut Roux-en-Y reconstruction. Gastric resection for AGC tends to be more extensive in order to get enough disease-free margin, and thus the tension on the BI anastomosis might be increased more than on the BII with Braun anastomosis or uncut Roux-en-Y anastomosis. This is thought to be the reason why anastomosis-related complications were higher in BI reconstruction than in other reconstructions in this study. Moreover, for BI reconstruction, the duodenum was transected extracorporeally after complete dissection, while for Roux-en-Y or BII reconstruction, the duodenum was cut before suprapancreatic dissection, and thus those procedures improved visibility of this area and suprapancreatic lymph node dissection could be performed more easily. In this regard, uncut Roux-en-Y or BII reconstruction may be a better option for reconstruction after LADG in AGC patients.

In conclusion, the rates of overall and local complications in this prospective study suggest that LG is applicable in treating AGC. However, the procedure should be performed cautiously in elderly patients. To reduce the complications after LADG in AGC patients, we recommend uncut Roux-en-Y or BII with Braun reconstruction. This result should be verified in a phase III trial.

Disclosures Ju-Hee Lee, Sang-Yong Son, Chang Min Lee, Sang Hoon Ahn, Do Joong Park, and Hyung-Ho Kim have no conflicts of interest or financial ties to disclose.

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