count data and follow a Poison distribution. Based on a negative binominal regression, the incidence rate ratio of postoperative stay, days with fever, and days to first flatus were 0.90 (95 % CI = 0.77–1.06; $P = 0.2$), 0.72 (95 % CI = 0.53–1.02; $P = 0.06$), and 0.7 (95 % CI = 0.55–0.87; $P < 0.001$), respectively.

Surgical parameters and postoperative blood and specimen analysis

Operative time was substantially longer in the LADG group (182.8 min) than in the ODG group (113.0 min). Blood loss was significantly lower in the LADG group (64.4 g) than in the ODG group (167.8 g). There was little difference between the groups with respect to the number of dissected lymph nodes (Table 3). Unexpectedly, there was no difference between the groups with respect to the IL-6 levels on postoperative days 1 and 3, while there were significant differences in WBC and CRP level on postoperative days 1, 3, and 7. Hemoglobin, total protein, and albumin levels did not differ between the groups on postoperative days 1, 3, and 7 (Table 4). Histopathological examination of the resected specimens revealed multiple cancers in seven patients, three in the LADG group and four in the ODG group. Histological types and tumor size were similar in both groups (Table 5). As for the depth of tumor invasion, 28 patients (90.3 %) in the LADG group and 31 patients (96.9 %) in the ODG group had early (mucosal or submucosal) gastric cancer. The rate of lymph node metastasis and disease stage according to UICC staging also did not differ between the groups

Discussion

This RCT was conducted because of recent drastic changes in the clinical management of gastric cancer. Many oncological studies have shown that a reduced lymph node dissection range is sufficient for clinical early gastric cancer [22, 25]. Moreover, postoperative adjuvant chemotherapy with annual administration of S1 was effective in Japan [26], where radiation therapy has not been established as postoperative adjuvant therapy as it is in the US [27]. The present 63 cases included only three advanced gastric cancer cases, so such adjuvant therapy may affect the long-term result very minutely in our study. On the other hand, the most critical factors affecting short-term clinical outcomes depend on development of surgical devices (same Harmonic Scalpels and anastomosing devices were used for the LADG and ODG groups), surgical skill, and postoperative management, including the application of a clinical path or pain control such as PCA.

Table 3 Surgical parameters

	LADG ($n = 31$)	ODG ($n = 32$)	P value
Operation time (min)	182.8 (SD = 37.7)	113.0 (SD = 21.1)	<0.001
Blood loss (g)	64.4 (SD = 48.9)	167.8 (SD = 135.3)	<0.001
Number of dissected lymph nodes	31.6 (SD = 12.2)	33.8 (SD = 13.4)	0.5

Until now, a substantial number of retrospective studies [13–15] and a modest number of RCTs [16–21] have compared laparoscopic surgery with open surgery, and, in general, the results have been in favor of laparoscopy. In Japan, the number of laparoscopic surgeries for gastric cancer is increasing every year [9], and techniques as well as surgical expertise have improved. To assess whether the improved surgical standards have an impact on the outcomes, an up-to-date randomized clinical trial was conducted. This article reports the short-term clinical outcomes of the trial and shows that laparoscopic surgery is associated with less pain, less use of analgesics, fewer complications, a quicker return of gastrointestinal function, and less fever. Long-term outcomes are to be formally reported in the near future.

In LADG and ODG, the technical expertise and experience of the operators have a strong influence on the time required for surgery, the volume of bleeding, and the accuracy of lymph node dissection. Therefore, the operators in the present RCT were restricted to expert surgeons in both techniques and operations were performed by a single gastrointestinal surgical group. The authors started performing LADG in September 1998 and the first case that was included in this RCT was the 163rd case at our facility. Shown in Supplementary Figs. 1 and 2 are our learning curve for LADG in terms of both operation time and blood loss up to the initiation of this study.

Similar to other reports [10–12], reductions in operative time and bleeding were obtained with increasing experience. In the six RCTs comparing LADG and ODG that have been conducted to date [16–21], the average time required for surgery was 196–378 min in the LADG group, with a large difference observed among institutions. The time was significantly longer in the LADG group compared with the ODG group for each RCT. Similar results were obtained in the present study, i.e., operative time was 182 min for LADG and 113 min for ODG, both of which are the shorter than any of the operative times reported in other studies (Table 6). The short operative times in the present study are thought to have been a result of the fact that the two expert surgeons (SS and KS) had performed 162 LADG procedures before the start of the RCT. Additionally, when one of the surgeons served as the operator, another surgeon served as the assistant. ODG was

Table 4 Postoperative blood analysis

	LADG (n = 31)	ODG (n = 32)	P value
IL-6 level			
Day 1	24.8 (SD = 19.2)	31.1 (SD = 19.6)	0.2069
Day 3	9.7 (SD = 8.8)	10.8 (SD = 8.2)	0.6429
WBC (/m^3)			
Day 1	8,326 (SD = 1921)	10,523 (SD = 2406)	0.0002
Day 3	7,274 (SD = 2129)	7,945 (SD = 2766)	0.2888
Day 7	5,430 (SD = 1468)	6,950 (SD = 2039)	0.0016
C-reactive protein (mg/dL)			
Day 1	3.1 (SD = 1.5)	4.9 (SD = 2.1)	0.0003
Day 3	5.1 (SD = 4.0)	7.7 (SD = 4.8)	0.0253
Day 7	1.4 (SD = 1.7)	3.1 (SD = 2.8)	0.0061
Total protein (g/dL)			
Day 1	5.71 (SD = 0.45)	5.57 (SD = 0.39)	0.1991
Day 3	6.42 (SD = 0.50)	6.29 (SD = 0.54)	0.3429
Day 7	6.51 (SD = 0.44)	6.60 (SD = 0.51)	0.4363
Albumin (g/dL)			
Day 1	3.46 (SD = 0.24)	3.38 (SD = 0.23)	0.2192
Day 3	3.85 (SD = 0.29)	3.77 (SD = 0.31)	0.3249
Day 7	3.93 (SD = 0.27)	3.96 (SD = 0.30)	0.6507

Table 5 Histopathological findings of the resected specimens

	LADG (n = 31)	ODG (n = 32)	P value
Multiple cancer			
Present	3	4	0.7215
Absent	28	28	
Tumor size (cm)	3.9 (SD = 2.0)	3.6 (SD = 2.4)	0.6412
Histological type			
Well-differentiated	9	16	0.0890
Poorly differentiated	22	16	
Depth of tumor invasion			
Mucosa	18	17	0.4436
Submucosa	10	14	
Muscularis propria	2	0	
Subserosa	1	1	
Lymph node metastasis			
Present	5	3	0.4209
Absent	26	29	
Disease stage[a]			
IA	26	28	0.5316
IB	3	4	
II	1	0	
IIIA	1	0	

[a] Disease stage was determined according to UICC staging

performed by a team of two surgeons that had performed more than 1,000 ODG procedures and a surgeon who had performed more than 500 ODG procedures.

The extent of bleeding in the present study was substantially less for the LADG group (64 g) than for the ODG group (168 g). It was also the least of all other groups in the six other RCTs [16–21]. A large volume of bleeding can cause poor visibility of the tissues that are to be dissected, thereby reducing accuracy in lymph node dissection. The volume of bleeding in the present ODG group was also less than the volumes reported in the six other RCTs [16–21]. It is thought that use of ultrasonically activated scissors contributed to less bleeding in the present ODG group.

Kitano et al. [28] reported that the VAS score was significantly lower after LADG than after ODG during rest, coughing, and walking. In the present study, the VAS when rising up from bed was lower in the LADG group, but there was no significant difference between the groups. The absence of a difference can be attributed to sufficient measures for alleviating pain, such as using suppositories and/or intramuscular injections of analgesic drugs for uncontrollable pain as well as by administering additional analgesic drugs through the epidural catheter. As expected, significant differences were observed between groups in terms of acute inflammatory parameters such as WBC and CRP. This is similar to that reported by Hayashi et al. [17] except that there was no significant difference in IL-6-level. In the present study, the operative time was shorter and there was less bleeding in both groups compared to those of other studies, which may have contributed to the absence of large differences in acute inflammatory parameters such as IL-6.

In the present study, the occurrence of postoperative complications was less frequent in the LADG group than in the ODG group, but the difference was not significant. Very recent meta-analyses concluded that there were significantly fewer postoperative complications in LADG than in ODG [29, 30]. These reports support the current results on postoperative complications. No postoperative complications were observed in the LADG group during the hospital stay after surgery, although in one case, anastomotic stenosis occurred 1 month after surgery. This patient recovered after balloon dilation of the anastomosis under gastroendoscopy. Five cases of postoperative complications were observed in the ODG group, including three major complications (bleeding in two cases and abdominal abscess in one case). Of the two cases with postoperative bleeding, a blood transfusion and an emergency operation were performed in one case due to shock caused by a large volume of active bleeding immediately after ODG. However, this was the only case requiring reoperation for hemorrhage in our institute within the last 5 years, and this suggested that such a basic and critical complication could not be completely avoided even by expert surgeons in ODG. Hemostasis was achieved following observation of the bleeding at the site

Table 6 Previous 6 RCTs' data information for operation time, blood loss, analgesics given, hospital stay, and complications

Ref.	Patient no.		Operation time (min)		*P* value	Estimate blood loss (ml)		*P* value	Times analgesics		*P* value	Hospital stay (day)		*P* value	Complications		*P* value
	LADG	ODG	LADG	ODG		LADG	ODG		LADG	ODG		LADG	ODG		LADG	ODG	
16	14	14	227	171	<0.05	117	258	<0.05	3.3	5	NS (dose; NS)	17.6	16	NS	2	4	NS
19	24	23	319	190	<0.001	336	294	NS	9.8	12.3	NS (epi; NS)	11.2	17.3	0.069	3	10	NS
17	14	14	378	235	<0.001	327	489	NS	0.8	2.1	NS (epi <0.001)	12	18	<0.001	nd	nd	
18	30	29	196	168		229	391	<0.001	nd	nd		10.3	14.5	<0.001	nd	nd	
20	82	82	253	171	0.001	112	267	0.001	39.ml	47.8 ml	0.019	7.2	8.6	0.0001	0	4	NS
21	179	161	nd	nd		109	200	<0.001	nd	nd		nd	nd		17	24	NS
Kitasato	31	32	182	113	<0.001	64	168	<0.001	14.6	21.5	0.022	9.1	10	0.2	1	5	NS

nd no data, *NS* not significant

adjacent to the left gastric artery. The patient's postoperative course was favorable, and the patient was discharged 12 days postoperatively. In the other bleeding case, although hemoglobin had decreased to 7.8 g/dL, the patient was discharged without blood transfusion 15 days postoperatively. In one case of abdominal abscess, the patient recovered after administration of antibiotics and was discharged 23 days postoperatively. Minor complications included a case of pneumonia and a case of wound infection. After mild relief was achieved conservatively, the two patients were discharged 13 and 12 days after surgery, respectively.

Lymph node metastasis of early gastric cancer occurs in 20 % of patients, but the 5-year survival rate is high (95 %) [31, 32]. The present study found that the mean number of resected lymph nodes was similar in the LADG and ODG groups. The resected margins were free from tumor, and radical treatment was achieved in all cases. The alternate primary long-term end point was patient prognosis in this study, which may be greatly affected by age over 75 years, which is near the average life span of males, the predominant sex affected by gastric cancer. Thus, patients over 75 years old were excluded from the present study. Four of the patients have already died due to diseases unrelated to gastric cancer (liver cancer-ODG, lung cancer-ODG, leukemia-ODG, and pancreatic cancer-LADG) at present (median follow-up = 69 months, range = 55–89 months), but no recurrence has occurred in either group. The final long-term result from this trial will be disclosed after February 20, 2013 (according to UMIN000001513).

Based on the present results, LADG and ODG can be considered techniques with good curability according to the latest Japanese treatment guidelines [23]. Given the results described above, we envision that LADG will come into use as an alternative to ODG in the near future. There were no cases of recurrence of lymph nodes beyond D1+alpha/beta in the present study, and the results were confirmed when all cases over 500 patients were included after the initial one [22], so that the use of preoperative PET-CT to stage the tumor prior to surgery is thought to be highly limited in cT1 gastric cancer.

Lastly, the limitations of the current study must be considered. No factors were allocated in this RCT, and the sex distribution was marginally biased (14/31 were females in the LADG group and only 7/32 were females in the ODG group, $P = 0.05$). This clinical difference might affect the results and interpretations.

In conclusion, the present randomized clinical trial comparing LADG and ODG performed by expert surgeons again demonstrated that LADG has several short-term advantages, including less pain, less bleeding, fewer serious complications, earlier recovery of bowel movements, and less systemic invasiveness. Although long-term outcomes still need to be formally addressed in the near future,

the present study suggests that LADG is a safe form of surgery for gastric cancer with good short-term curability.

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ORIGINAL ARTICLE

Survival outcome of laparoscopic gastrectomy for clinical early (cT1) gastric cancer

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Abstract
Purposes Laparoscopy-assisted gastrectomy (LAG) for clinical early (cT1) gastric cancer (EGC) is superior to open gastrectomy in terms of the short-term outcome; however, long-term survival outcome remains elusive.
Methods Four hundred and ninety-one cT1 EGC patients who underwent LAG between 1998 and 2010 were registered to evaluate the survival outcome, including 237 patients who were observed for at least 5 years (long-term, L group), while 221 patients who were observed for at least 2–5 years (intermediate term, I group).
Results There were 17 deaths, including 7 patients who developed recurrence (5 in pT1 and 2 in pT4a). Two fatal cases with pStage IIB were uniquely T1N3b. Six out of the 7 recurrences occurred within 2 years after surgery. The 237 patients in the L group included 6 of the recurrent deaths (2.5 %), while the 221 patients in the I group included 1 recurrent death (0.9 %). Recurrent sites of pathological T1 cases were the liver ($n = 2$), lung ($n = 1$), ovary ($n = 1$), and bone ($n = 1$), and no peritoneal or local recurrence was found.
Conclusions Collectively, the survival outcome of EGC by LAG was excellent and LAG was acceptable as a therapeutic procedure for EGC.

Keywords Laparoscopy-assisted gastrectomy · Long-term survival outcome · Early gastric cancer · Recurrence

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Introduction

Laparoscopy-assisted gastrectomy (LAG) for early gastric cancer (EGC) was introduced by Kitano and colleagues [1]. The number of patients undergoing LAG has been increasing rapidly in Japan [2], where there is a high incidence of EGC due to a rigorous surveillance system for EGC. Improvements in instruments and laparoscopic technique have resulted in widespread acceptance of LAG, not only for distal gastrectomy but also for other types of resection, such as proximal gastrectomy [3] and total gastrectomy [4, 5]. The advantages of LAG over conventional open resection include reduced postoperative pain, earlier recovery, a shorter hospital stay, and better cosmesis [2, 6]. LAG is less invasive and inflammatory, and a recent report suggested that the inflammation may affect the long-term outcome in gastric cancer [7].

Although there is high-quality evidence to support the short-term efficacy of LAG for EGC, there are few accounts of the long-term survival [6, 8–10]. Detailed and organized accounts of the long-term oncological efficacy of LAG could promote this approach as the primary treatment for EGC. This report presents the long-term oncological outcomes from LAG, including all patients treated from the beginning of the application of laparoscopic surgery to determine the long-term effectiveness and patient survival in a single institute.

Methods

Patients

Two thousand and three patients with gastric cancer were managed surgically at the Department of Surgery in the

Kitasato University Hospital from September 1998 to August 2010, including 541 patients treated with LAG. Four hundred and ninety-one of the 541 patients were preoperatively diagnosed as cT1. Preoperative staging was based on double-contrast upper gastrointestinal X-ray series, gastric endoscopy, abdominal ultrasound sonography (echo), and enhanced computed tomography (CT). The initial indications for LAG at this institute include all tumors confined to the early lesions (cT1) with subsequent transition to the muscularis propria (cT2N0 since February 2003 and cT2N1 since March 2008). Patients requiring additional surgery after suspicious incomplete endoscopic resection are also included. Serosal invasion (SE) was not indicative for LAG. There were no patients who had had such intraoperative findings (surgical SE) in this current study due to careful patient selection.

Surgical indications and procedure

The type of gastric resection was determined according to the tumor location, size, and depth of invasion. Modified lymphadenectomy (D1 + alpha/beta) for EGC is based on Japanese treatment guidelines [11]. LAG was classified into 4 groups; laparoscopic-assisted distal gastrectomy (LADG, $n = 333$), laparoscopy-assisted proximal gastrectomy (LAPG, $n = 54$), laparoscopy-assisted pylorus-preserving gastrectomy (LAPPG, $n = 44$), and laparoscopy-assisted total gastrectomy (LATG, $n = 60$).

The history of LAG in this institute is shown in Fig. 1 (including LAG with cT1 and others). LADG was introduced in September 1998 [2] and LAPG (since November 1999) was indicated for EGC close to the cardia in the upper third of stomach with no evidence of lymph node involvement, and Toupet-like partial fundoplication was added in order to reduce gastro-esophageal reflux disease in November 2005 [3]. The indications for LATG (since July 2003) were cT1 lesions over 3 cm close to the cardia

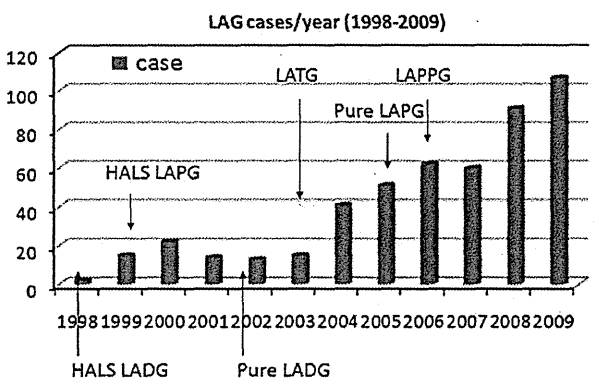

Fig. 1 History of LAG development and annual numbers of LAG for gastric cancer (both EGC and AGC) in this institute between 1998 and 2009

that is obscure in border, larger than 5 cm in diameter or multiple lesions for which the distal stomach cannot be preserved are absolute indications [4]. LAPPG has been indicated for greater curvature lesions of the lower body of the stomach limited to the mucosa below 3 cm in diameter since April 2006.

The patient was positioned with the hips extended and abducted for the camera operator between the legs, and primary surgeon initially stands on the right side of the patient. Pneumoperitoneum of 8 mm Hg was established through a supra- or infra-umbilical trocar for the camera port and liver elevation was achieved using a snake retractor. Greater curvature mobilization was performed by dividing the gastrocolic ligament 3–4 cm away from gastroepiploic vessel arcade. The left gastroepiploic vessels (LN-lymph node-station #4sb) were divided to reach the proximal resection line distally through the avascular area between the left gastroepiploic and short vessels, and the distal mobilization was performed up to the duodenum by cutting the prepancreatic fascia and the right gastroepiploic vessels (#6) were exposed. The right gastric vessels (#5) were divided after the exposure of gastroduodenal artery and the left gastric vessels were divided with preservation of the celiac branch of the vagal nerve. The lesser curvature was cleared of its perigastric fat around both the #1 and #3 LN stations before gastric transection in case of LADG or LAPPG. Lymph node dissection was performed during vascular mobilization according to guidelines for taking lymph nodes en bloc on the side of the resection. D1 + alpha (#7) lymph node dissection was performed for cancer limited to suspicious mucosal lesions, and D1 + beta (#7, 8a, and 9) was performed for those thought to extend submucosally. The cut line was determined by preoperative clipping, which was intraoperatively confirmed by palpation by the surgeon. The specimen was retrieved from small midline incisions between 4 and 6 cm in length. Reconstruction was by either Billroth-I or Roux-en-Y, as determined by the size of remnant stomach and the potential for tension with a gastroduodenostomy. Intracorporeal anastomoses were fashioned using endoscopic linear staplers or circular staplers (Orvil was used since November 2007) in LAPG [3].

The resection margin was histologically confirmed to be cancer-negative for all cases. Preoperative clipping near the cancer lesions was performed for suspicious cases to prevent margin-positive judgment [12]. Four cases were converted from LADG to LATG due to positive margins.

Follow-up

Histological staging was determined according to the 14th edition of the Japanese Classification of Gastric Cancer (JCGC) stage classification criteria [13]. All patients with

pathologically diagnosed EGC were followed up to examine tumor markers (CEA, CA19-9, and CA125) at least every 6 months for 5 years. Upper gastrointestinal endoscopy (UGI), abdominal sonography (US), and abdominal CT were carried out annually for 5 years. Patients with pathologically diagnosed advanced gastric cancer were followed up to examine tumor markers (CEA, CA19-9, and CA125) at least every 3 months for 5 years. UGI, US, and CT were carried out at least annually. US and CT were also examined twice a year for 3 years in pathologically diagnosed Stage III. Adjuvant chemotherapy in the form of S-1, an oral fluoropyrimidine, was administered for 1 year in patients with stage II/III according to the ACTS-GC trial [14].

Statistical analysis

All statistical tests were performed using the Stat View software package, version 5 (SAS Institute Inc., Cary, NC). Differences in categorical variables, such as postoperative complications, tumor recurrence, and other clinicopathological factors were analyzed by the Chi-square test and p value <0.05 was considered significant. All continuous data are presented as the mean ± standard deviation.

Results

Patient characteristics

The demographic, surgical, and clinicopathological characteristics of cT1 EGC patients undergoing LAG are presented in Table 1. The Japanese Gastric Cancer Association (JGCA) stages (14th edition) of the patients were stage IA ($n = 431$), stage IB ($n = 29$), stage IIA ($n = 12$), stage IIB ($n = 8$), stage IIIA ($n = 5$), stage IIIB ($n = 5$), and stage IIIC ($n = 1$) in cT1 EGC patients. There were no cases with a positive cytology test, thus the 14th JCGC stage was perfectly consistent with 7th UICC in this study.

Table 1 Demographic, surgical, and clinicopathological chacteristics in 491 cT1 EGC

Patients	Distribution
Age (years of age)	63.1 ± 11.2
Gender, male/female	335/156
Body mass index	22.7 ± 3.4
Operation (ADG/LAPG/LAPPG/LATG)	333/54/44/60
Lymph node dissection (D1 + alpha/D1 + beta)	122/369
Dissected lymph nodes	33.8 ± 16.3
Resection of other organs, yes/no	61/430
Operation time	273.5 ± 70.3
Bleeding	110.7 ± 146.1
Tumor location (U/M/L)[a]	91/265/135
Histology, intestinal/diffuse[b]	270/221
Tumor size	3.7 ± 2.3
UICC T factor (T1a/T1b/T2/T3/T4a)	240/210/23/11/7
UICC N factor (N0/N1/N2/N3a/N3b)	447/24/11/5/4
7th UICC stage, IA/IB/IIA/IIB/IIIA/IIIB/IIIC	431/29/12/8/5/5/1

[a] Tumor location represents that for the largest tumor if there are multiple lesions

[b] Histology represents that for the largest tumor if there are multiple lesions

Surgical morbidity and mortality

Table 2 summarizes the postoperative complications according to type of resection. Postoperative complications occurred in 31 patients (6.3 %). Postoperative complications after LATG and LAPG were similar, although anastomotic leakage was putatively more common in LAPG due to more inclusion of the anastomosis by the linear stapler (this procedure at present is no longer used, and no anastomotic leakage occurred with anastomosis by a circular stapler). No severe pancreatitis ($n = 0, 0$ %) occurred as reported in a recent publication [9]. Anastomotic or duodenal stump leakage occurred in 5 patients (1.0 %). Leakage of esophageal anastomosis using a circular stapler and linear stapler through a mini-laparotomy occurred in 0 and 2 (for LAPG), respectively. One patient with leakage who underwent LAPG required reoperation for the collection of percutaneous drainage in the mediastinal space. One patient with leakage had duodenal stump leakage after LATG. Postoperative gastric stasis did not occur in patients treated with LAPPG, presumptively due to the preservation of both subpyloric vessels and the first branch of right gastric vessels to avoid notorious stasis; however, food stasis was often observed by gastric fiberscopy during the follow-up after emission. Three patients experienced postoperative hemorrhage associated with the Y limb ($n = 1$), and unknown origins (oozing from drainage tube) in LADG ($n = 2$, 1 case of the latter is needed for transfusion). No patients died postoperatively (0 %), and no patients experienced severe complications associated with death, such as ARDS or severe pancreatitis.

Long-term and intermediate-term survival outcome of cT1 EGC by LAG

The median follow-up term was 49 months (range 19–161 months). Seventeen of the 491 patients with cT1 died during the follow-up period, including 7 recurrent cases (2 in pStage IA, 1 in pStage IB, 2 in pStage IIB, 1 in pStage IIIA, and 1 in pStage IIIB), all of which were cT1 treated by D1 + beta lymph node dissection (Table 3). The

Table 2 Intraoperative and postoperative complications in 491 cT1 patients undergoing laparoscopic gastrectomy

Complications	Type of resection			
	LADG (n = 333)	LAPPG (n = 44)	LAPG (n = 54)	LATG (n = 60)
Postoperative morbidity	22	0	3	6
Anastomotic leakage (n)	2	0	2	1
Anastomotic stricture (n)	4	0	0	2
Anastomotic ulcer (n)	0	0	0	0
Anastomotic bleeding (n)	0	0	0	1
Stasis (n)	0	0	0	0
Bleeding (n)	2	0	0	0
Bowel obstruction (n)	1	0	0	0
Wound infection (n)	3	0	0	1
Pulmonary infection (n)	3	0	0	0
Cholecystitis (n)	2	0	0	0
Cholangitis (n)	1	0	0	0
Phlegmatitis (n)	1	0	0	0
GERD (n)	0	0	1	0
Abscess (n)	2	0	0	0
Diarrhea (n)	1	0	0	1
Postoperative mortality	0	0	0	0
ARDS (n)	0	0	0	0
Severe pancreatitis (n)	0	0	0	0

NS no significant difference, *GERD* gastro-esophageal reflux disease, *ARDS* adult respiratory distress syndrome, *LADG* laparoscopy-assisted distal gastrectomy, *LAPPG* laparoscopy-assisted pylorus-preserving gastrectomy, *LAPG* laparoscopy-assisted proximal gastrectomy, *LATG* laparoscopy-assisted total gastrectomy

Table 3 Clinical features of recurrence death after LAG

Case	Sex	Age	Histology	pTNM	pStage	Size (cm)	ly	v	Operation	Dissection	Recurrent site	Recurrent (months)	Death (months)
1	M	78	Diffuse	pT1bN0M0	IA	1.5	0	2	LADG	DI + beta	Liver	7	26
2	M	71	Diffuse	pT1bN0M0	IA	2	1	2	LADG	DI + beta	Lung	48	64
3	M	64	Intestinal	pT1bN1M0	IB	4.5	1	0	LATG	DI + beta	Liver	12	24
4	F	41	Diffuse	pT1aN3b	IIB	2.4	0	0	LATG	DI + beta	Ovary	17	47
5	F	68	Diffuse	pT1bN3b	IIB	4.8	1	0	LAPG	DI + beta	Bone	12	51
6	M	56	Diffuse	pT4aN1	IIIA	25	1	0	LATG	DI + beta	Peritoneum	21	32
7	M	78	Intestinal	pT4aN2	IIIB	3	3	3	LATG	DI + beta	Peritoneum	3	6

LADG laparoscopy-assisted distal gastrectomy, *LATG* laparoscopy-assisted total gastrectomy, *LAPG* laparoscopy-assisted proximal gastrectomy

other causes of death (n = 10) included another primary cancer in 5 (3 with pancreatic cancer, 1 with sigmoid colon cancer, and 1 with hepatocellular cancer), a traffic accident in 1, internal hernia in 1, and other benign diseases in 3.

Six out of the 7 recurrent cases showed signs of recurrence within 2 years (Table 3), and the following 2 groups were observed in detail; 237 patients who were observed for at least 5 years (long-term group, L group), and 221 patients observed for 2 years to 5 years (intermediate-term group, I group). The L group included 41 patients who were lost to follow-up within 5 years (17.3 %) due to hospital transfer or personal reasons; however, the 29 patients actually visited until the 2-year follow-up. On the other hand, the I group included 14 patients who were lost to follow-up within 3 years (10.2 %) due to hospital transfer or personal reasons; however, 7 patients were followed until the 2-year follow-up.

The 237 cases with cT1 treated by LAG in the L group included 6 recurrent deaths (2.5 %), although 10 pathological advanced gastric cancer (pT2 in 8, pT3 in 1, and pT4a in 1) were included. The 6 recurrent cases actually corresponded to those listed in Table 3. Case 4 and 5 patients showed a unique prognostic pattern for cT1 EGC patients by LAG. Both cases were stage IIB that were T1N3b (node metastasis numbers were 39 and 18, respectively), and were the only T1N3b among the 491 patients. Case 4 showed a Kruckenberg tumor recurrence at 17 months after surgery. The patient with bone metastasis (case 5) recurred at 12 months after surgery.

The 221 cT1 cases in the I group showed only 1 recurrent death (0.5 %), and included 13 pathological AGC (pT2 in 8, pT3 in 4 and pT4a in 1).

Discussion

Several prospective trials have actually demonstrated that LAG is superior to open surgery, because there is less postoperative pain, faster recovery, and better cosmetic results [6, 15, 16]. In addition, the current study aimed to reveal the long-term survival outcome of LAG in the treatment of EGC. The short-term results showed surgical morbidity and mortality rates of 6.7 and 0 %, respectively, and these rates are consistent with previous reports in which the complication rates ranged from 2.5 to 26.7 % [6, 15, 16]. Pancreatic inflammation was recently described to be secondary to laparoscopic energy devices transmitting heat and causing severe pancreatic injury during radical lymph node dissection [9]; however, this complication did not occur in the 541 patients in the current series.

The current study showed excellent long-term survival in EGC patients treated by LAG. This result is consistent with other reports of long-term survival outcome by LAG [6, 8, 9], and supports the oncological efficacy as well as short-term outcome in comparison to open resection in EGC. Kitano and colleagues [6] reported a multicenter retrospective study of 1,294 LAGs in 16 institutions that showed that the 5-year disease-free survival rate is 99.8 % for stage IA disease, 98.7 % for stage IB disease, and 85.7 % for stage II disease with a median follow-up of 36 months. On the other hand, a report by Fujiwara and colleagues of a single center study of 94 LAGs for EGC found that the morbidity and mortality rates are 22.3 and 0 %, respectively, and overall survival rate is 90.1 % [17]. The present study found that the rate of cancer recurrence (Table 3) was similar to that in another prognostic reports of EGC in which recurrence developed in only 5 patients with EGC (1 liver, 1 bone, 1 locoregional and 2 peritoneum) [9]. Interestingly, neither regional lymph node nor locoregional recurrence was observed in the current series with cT1.

There were only 6 recurrent deaths among the initial 237 cT1 patients (L group, 2.5 %) who were followed up for over 5 years. The 6 recurrences were recognized in 2 pStage IA (pT1N0) patients, 1 pStage IB (T1N1), 2 pStage IIB (pT1N3b), and 1 pStage IIIB (pT4aN2) (Table 3). Most recurrences were recognized within 2 years after operation. There is only 1 patient recurrence (pStage IIIA; pT4aT1) in the 221 cT1 patients (I group) who were followed up for at least 2–5 years. Therefore, long-term survival was excellent if the survival analysis was restricted to pStage IA or pStage IB, as reported in previous RCT trials [6]. Two out of the 431 pStage I cT1 EGC patients treated by LAG (0.46 %), and 1 of the 29 pStage IB patients experienced recurrence (3.4 %). Such excellent clinical outcome of patients with pStage IA or pStage IB is consistent with a previous retrospective analysis of long-term survival of EGC treated by open surgery [18].

On the other hand, the 4 recurrences among 2 patients with pStage IIB (both T1N3b) and 2 patients with pT4a are considered to be concerned. Two cT1 EGC patients treated by LAG (10 %) out of the 20 pStage II (IIA/IIB), and 2 patients (18.2 %) of the 11 pStage III (IIIA/IIIB/IIIC) showed recurrence. This survival result is comparable or better than the corresponding outcome with conventional open surgery. This may be because the previous report showed that cT1 with pathologically advanced gastric cancer shows better prognosis among macroscopically predicted true AGC [19, 20]. The 2 former cases with pT1N3b were unique and rare clinical entities even in EGC, and the mortality among such patients in the current study was 100 % (2/2). Initial recurrent sites for both cases were in the ovary and bone, suggesting that such patients would not have been rescued, even with D2 lymph node dissection. However, the accumulation of more clinicopathological data is needed for such unusual cases in order to determine the optimal treatment.

This clinical practice conducts extensive preoperative diagnosis to avoid inadvertent inclusion of pT4a in cT1; nevertheless, 7 cases with pT4a (1.4 %) were included among the 491 cT1 patients and those included 2 recurrent cases, and longer follow-up could increase that to 2/7 (28.6 %) in the future. The most critical issue in this study was the underestimation of the preoperative diagnosis; however, the inclusion of advanced cancer in cT1 cases treated by LAG was 8.4 % (41 out of 491) in the present study, and this is consistent with previous reports (8.8 %) [9], and the diagnostic accuracy may also be standard. The recurrent sites of 2 fatal pT4a recurrent cases treated by LAG with D1 + beta lymph node dissection were both the peritoneum, so additional lymph node dissection may be ineffective for inhibiting such recurrence.

In conclusion, LAG for EGC appears to be a safe and feasible surgical procedure with acceptable short-term surgical and long-term oncological outcomes. These data suggest that LAG should be considered an optional primary treatment for patients with EGC; however, patients with cT1 with pN3b or pT4a must be considered to be at high risk for developing a fatal recurrence.

Conflict of interest There are no conflicts of interest associated with this study.

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ORIGINAL ARTICLE

Single-institute prospective trial of laparoscopy-assisted distal gastrectomy with systemic lymph node dissection for early gastric carcinoma

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Abstract
Background Laparoscopy-assisted gastrectomy (LAG) is an advanced surgery that requires the mastery of complex surgical skills. We evaluate the feasibility of LAG with systemic lymph node dissection when participating surgeons have sufficient knowledge and experience to conduct open surgery for gastric cancer and basic laparoscopic skills.
Methods All operations were performed by two Japan Surgical Society board-certified attending surgeons who had performed over 50 conventional gastrectomies and 30 laparoscopic cholecystectomies. The surgeons went through an established program, including training at the wet and dry laboratories. In addition, surgeries for the first 10 cases were assisted by an expert surgeon with experience of >300 cases. To be eligible for the LAG procedure, patients had to have a preoperative diagnosis of T1, N0 and M0 gastric carcinoma. The morbidity rate was used as the study endpoint. Variables such as operating time, intraoperative blood loss and number of retrieved lymph nodes were evaluated as complementary surgical endpoints. These variables were compared between the first 25 cases and the latter 25 cases.
Results A total of 50 patients who were scheduled to undergo LAG were prospectively enrolled between 2005 and 2008. Morbidity rate was 4% (2/50), with one case due to intestinal injury and one case due to an intra-abdominal abscess. Complications related to laparoscopy were observed in 2% (1/50), with one case of mesenteric injury. The conversion rate to laparotomy was 6% (3/50). However, there were no serious consequences in converted cases. The operating time was 263.7 ± 45.0 min. The intraoperative blood loss was 94.5 ± 106.5 g. The total number of regional lymph nodes retrieved was 34.7 ± 12.2. A significant improvement in the blood loss was only noted after the first 25 procedures. All patients are alive and disease-free after a median follow-up of 38.8 months.
Conclusion An adequate training program, including site visits by expert surgeons, in conjunction with basic laparoscopy skills and solid backgrounds in open gastrectomy from the perspective of the trainees are currently key to the successful and safe implementation of LAG. Whether the procedure is oncologically feasible remains to be confirmed by long-term follow-up.

Keywords Gastric carcinoma · Laparoscopy-assisted gastrectomy · Prospective trial · Surgical training · Surgical background

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Introduction

In the past decade, laparoscopic techniques have gained wide clinical acceptance in surgical practice. The important advantages offered by this approach, as compared to the open surgery procedure, include reduced intraoperative blood loss, reduced postoperative pain and accelerated recovery, earlier return to normal bowel function with

earlier resumption of oral intake, and earlier discharge from the hospital. These potential benefits observed for laparoscopic cholecystectomy have prompted surgeons to expand this approach to other procedures, including the resection of neoplastic diseases. Laparoscopic surgery is considered the criterion standard for the treatment of several benign diseases and some malignant diseases such as colon cancer [1]. However, laparoscopic-assisted gastrectomy (LAG) for gastric cancer has yet to be validated, for several reasons. First, LAG with systemic lymph node dissection is technically quite difficult to perform. In addition, LAG has only been performed by a limited number of surgeons dedicated to laparoscopic surgery. Finally, few reports have described the advantages of performing LAG for early gastric cancer, and most of these were retrospective case series of a limited number of patients. Thus, LAG is not applicable as a standard treatment for gastric cancer. At the present time, the Japanese Gastric Cancer Association (JGCA) states that LAG should be performed only in a clinical trial setting in accordance with their gastric cancer treatment guidelines [2].

Since laparoscopic surgery has been proven to have substantial advantages over conventional surgery, it is foreseeable that LAG will gain significance in the future and will eventually be regarded as a standard of care. As far as it goes, LAG requires abilities well beyond the basic technique and knowledge of laparoscopic surgery in order to conduct clinical trials safely. In the current study, we prospectively evaluated our experience of implementing this procedure in a high-volume hospital, which involved adhering to a strict training program and working under the guidance of an established expert in this field, while maintaining basic ethical principles. Our aim was to show that the technique used to perform LAG can be acquired safely under an adequate instruction and training program; it is not possible at this time to show that this surgery is oncologically equivalent to the open surgery.

Patients and methods

Patients

Between August 2005 and March 2008, we enrolled 51 consecutive patients for LAG with lymph node dissection. Demographic, clinical, operative, and pathologic data were collected. Eligibility criteria were as follows: performance status of ECOG 0–1; age range between 20 and 75 years old; histologically proven gastric adenocarcinoma; location of the primary tumor within the lower and middle third of the stomach; presence of cT1, cN0 and cM0 as diagnosed by endoscopy, barium study and CT; sufficient organ function; and written informed consent.

Surgeons

To be considered capable of performing LAG, surgeons were required to be board-certified by the Japan Surgical Society, to have performed at least 50 open gastrectomies with lymph node dissection, and to have completed at least 30 laparoscopic cholecystectomies. In addition, surgeons had to be trained in the Nagoya University Endoscopic Surgery (NU-ESS) training laboratory and animal laboratory in accordance with the Nagoya University School of Medicine, Surgery II Educational Program for LAG. This educational program consisted of three components: (1) suturing training in the box trainer; (2) virtual reality (VR) simulator training using MIST (SimSurgery, AS, Oslo, Norway), the Lap Sim System (Surgical Science Ltd, Gothenburg, Sweden), and Lap Mentor (Simbionix Corporation, Cleveland, OH, USA), and; (3) a hands-on training course for LAG in a porcine model. Of the three VR simulators, MIST was mainly used to improve suturing skills. The Lap Sim System consists of 11 different exercises featuring camera navigation, instrument navigation, hand coordination, grasping, cutting, clip applying, lifting and grasping, suturing, precision and speed, handling intestines, and fine dissection, and was used to teach a wide range of basic skills. Lap Mentor offers training in complete laparoscopic surgical procedures through virtual reality laparoscopic cholecystectomy. We were required to participate in the NU-ESS training scheme twice within 1 year before starting the study.

Procedures

Two board-certified surgeons (Y.M. and S.I.) were chosen to operate on the trial patients. Ten initial operations were supervised by an experienced mentor who had acquired the Endoscopic Surgical Skill Qualification and has performed >300 laparoscopy-assisted gastrectomies (M.F.). All operations after the first 10 were performed by either of the two surgeons, while the other surgeon invariably took part as an assistant. A total of 6 surgical residents who rotated the group for 6 months during the study period handled the video scope. These residents also had experience of at least 10 open gastrectomies as either surgeon or assistant. LAG was performed according to a previously published approach [3]. Lymph node dissection and ligation of vessels were carried out in the laparoscopic field. Lymphadenectomy was performed according to the JGCA guidelines. Laparoscopy-assisted pylorus-preserving gastrectomy (LAPPG) was only indicated for mucosal carcinoma located in the middle third, while laparoscopy-assisted distal gastrectomy (LADG) was used in the remaining early carcinoma cases. The gastrectomy and subsequent gastroduodenostomy used the same methodology employed in open surgery, with the procedure performed through a 4-cm midline skin incision window.

Endpoints

Morbidity rate was used as the study endpoint. We hypothesized that the lower limit of the 95% CI for the observed morbidity rate would not exceed the historical control morbidity rate of 11.6%, which is the rate that was calculated for the 1153 cases of open distal gastrectomy with systemic lymph node dissection performed between 1994 and 2003 at our institute.

Other perioperative outcomes, including operating time, intraoperative blood loss, conversion rates, and retrieved lymph nodes, were evaluated and also adopted as learning indicators. The learning curve was defined as the comparison of the first 25 procedures with the second 25.

Ethics

Written informed consent was obtained from all patients participating in the study.

The study protocol was approved by the Institutional Review Board of the Aichi Cancer Center Hospital. The trial was overseen by an independent data monitoring committee.

Results

Clinicopathological characteristics of the patients

A total of 50 patients (31 men and 19 women; mean age ± standard deviation, 57.4 ± 10.8; mean body mass index, 21.9 ± 2.9) who were scheduled to undergo LAG were prospectively enrolled between 2005 and 2008. Three of these 50 patients had undergone a previous surgery. Details of the surgical procedures and the pathologic data are presented in Table 1.

Table 1 Surgical procedures and pathological data

Variables	No. of cases
Surgical procedure	
LADG	40
LAPPG	8
LADG + cholecystectomy[a]	2
Lymph node dissection	
D1 + alpha	16
D1 + beta	34
Tumor location	
Middle third	38[b]
Lower third	18[b]
Lower-middle third	1[b]
No. of primary tumors	
Solitary	43
Multiple	7
Depth of invasion	
T1 (mucosal)	28
T2 (submucosal)	20
T3 (muscle propria)	2
Lymph node metastasis	
N0	47
N1	1
N2	2
Distant metastasis	
M0	50
M1	0
Stage	
IA	46
IB	2
II	1
IIIA	1

[a] Contributed to cholecystectomy for co-existing cholelithiasis

[b] Number of lesions

Surgical outcomes

The mean operating time was 263.7 ± 45.0 min. The average amount of blood loss during the surgery was 94.5 ± 106.5 mL. None of the patients required any transfusions during or after the operations. The total number of regional lymph nodes retrieved was 34.7 ± 12.2 (range 30–46).

A complication related to the laparoscopy occurred in one case and included injury of the transverse colon mesentery. The situation was resolved intra-operatively without any hardship or further critical complications. In another case, there was a postoperative complication involving an intra-abdominal abscess on the anterior surface of the head of the pancreas, which was treated conservatively. The overall morbidity rate was 4% (2/50). The lower limit of the 95% CI for this morbidity rate did not exceed the historical control morbidity rate. A total of three (6%) out of the 50 cases required conversion to laparotomy due to uncontrollable bleeding ($n = 1$), injury of the transverse colon mesentery ($n = 1$) or other disease at the lesser curvature of the remnant stomach, which turned out to be suspicious for gastrointestinal stromal tumor by frozen section ($n = 1$). All three cases were restored by open surgery, and none of the patients developed any postoperative complications. There was no difference in operating time, blood loss, and the incidence of postoperative complications between these patients and those whose surgeries were completed by the laparoscopy-assisted approach. There were no deaths related to the laparoscopic surgery; nor were there any operative or in-hospital deaths. All patients are alive and disease-free after a median follow-up of 38.8 months.

Comparison of the first 25 procedures with the second 25

A comparison of the perioperative outcomes of the first 25 procedures with the second 25 is shown in Table 2. No significant difference was observed with the exception of the mean estimated blood loss, which decreased significantly from 125.8 to 63.2 g. No trend towards shorter operating time can be seen in Fig. 1.

Discussion

Laparoscopic cancer surgeries that require advanced skills are now considered to be an acceptable alternative to open surgery in patients with colorectal cancer [1]. Prospective randomized studies have demonstrated that both short- and long-term outcomes after laparoscopic resection for colorectal cancer are comparable to those observed for the open approach [4–6]. This has led the American Society of Colon and Rectal Surgery to issue a statement approving the procedure [7]. However, laparoscopic surgery has yet to be validated for gastric cancer and is thus only performed in a limited number of gastric cancer patients. In addition, many of these previous studies were retrospective, and therefore, while they are informative, the conclusions drawn can only be viewed as preliminary. In addition, LAG with lymphadenectomy is a complex procedure and requires not only advanced laparoscopic skills but also skills in performing open gastrectomy procedures. As a result, the JGCA currently does not endorse LAG in a curative cancer resection setting outside of clinical trials due to concerns over potentially compromised cancer control [2].

Table 2 Comparison of postoperative outcomes between first 25 cases and second 25 cases

	First 25 cases	Second 25 cases	*P*
Ope. time (min, mean ± SD)	268.4 ± 45.1	258.9 ± 45.4	NS
Blood loss (g, mean ± SD)	125.8 ± 113.6	63.2 ± 90.6	0.03
No. of LN (no., mean ± SD)	35.0 ± 9.2	34.4 ± 14.8	NS
Morbidity (%)	1 (4)	1 (4)	NS
Mortality (%)	0	0	NS
Conversion (%)	2 (8)	1 (4)	NS

Ope. time operating time, *blood loss* intra-operative blood loss, *no. of LN* number of retrieved lymph nodes

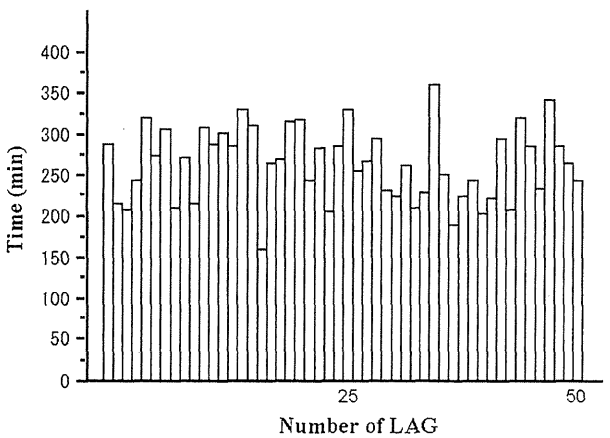

Fig. 1 Operating time for LAG

However, because of substantial advantages such as less pain, more rapid recovery of bowel function, and better cosmetic results, LAG has rapidly gained popularity for gastric cancer in Japan. We believe that a solid background in both gastrectomy and basic laparoscopic technique is required before surgeons can ethically and safely perform LAG.

Several previous reports have examined the relationship between board certification and surgical outcome. Prystowsky et al. [8] reported that American Board of Surgery certification was associated with reduced mortality and morbidity for colorectal resection. Pearce et al. [9] found that surgeons with a subspecialty certification had better outcomes for carotid endarterectomy and abdominal aortic aneurysm repair. More interestingly, Avital et al. [10] reported that adequate oncologic resections in laparoscopic treatment might be achieved earlier, provided that surgeons adhere to open standard cancer resection methods. Ryu et al. [11] also indicated that the learning period for LAG could decrease when participating surgeons had substantial experience of open gastric surgery. Parikh et al. [12] provided data on the learning curve for open gastrectomy with lymphadenectomy, and postulated that the operator should have performed more than 25 of these procedures under supervision before being considered to be competent in this technique. We assumed, therefore, that experience of 50 cases as an operator would be sufficient for the surgeon to have acquired sufficient technical skills to perform open gastric cancer surgery. Since both of the surgeons that participated in the current study were not only board-certified by the Japan Surgical Society but they also had more than sufficient experience in open gastrectomy, they were defined here as having a solid background in gastric cancer surgery.

Since LAG is a very demanding procedure from a technical point of view, adequate training in laparoscopic techniques and methodology is mandatory. Following training in wet and dry laboratories, several studies have demonstrated improved performance with a significant learning curve [13–16]. In the current study, the surgeons, in accordance with the Educational Program for LAG at

Table 3 Comparison of outcomes in case series of LAG

Year	Author	Pros./retro.	No.	Ope. time (min)	Blood loss (g)	No. of LN	Mortality (%)	Morbidity (%)	Conversion (%)
2000	Shimizu [18]	Retro.	21	299 ± 61	273 ± 200	14 ± 10	0	19	4.7
2002	Kitano [19]	Pros.	14	227 ± 7	117 ± 30	20 ± 4	0	14	0
2003	Fujiwara [3]	Pros.	43	225 ± 56	239 ± 322	20.2 ± 9.9	0	16.2	2.3
2005	Hayashi [20]	Pros.	14	378 ± 97	327 ± 245	28 ± 14	0	0	0
2005	Huscher [21]	Pros.	30	196 ± 21	229 ± 144	30 ± 14.9	3.3	23.3	–
2006	Ziqiang [22]	Retro	44	255 ± 46	147 ± 109	30.1 ± 16.9	0	13.6	2.2
2007	Lee [23]	Pros.	64	280	196	50.1	0	3.1	6.6
2008	Ryu [11]	Retro.	347	270 ± 59	–	–	0	9.8	2.3
2009	Our study	Pros.	50	263.7 ± 45.0	94.5 ± 106.5	34.7 ± 12.2	0	4	6

LAG laparoscopy-assisted pylorus-preserving gastrectomy and laparoscopy-assisted distal gastrectomy, *pros.* prospective study, *retro.* retrospective study, *no.* number of patients, *ope. time* operating time, *blood loss* intra-operative blood loss, *no. of LN.* number of retrieved lymph node

Department of Surgery II, went through an intensive training course consisting of simulator training and at least three sessions of hands-on training with animals, and obtained basic skills by performing laparoscopic cholecystectomies. Although there is currently no strong evidence to indicate that performing cholecystectomies laparoscopically prior to proceeding to more advanced surgery is beneficial, it is reasonable to assume that the skills acquired during one laparoscopic procedure are transferable to another laparoscopic procedure. Since the experience of 30 laparoscopic cholecystectomies was required to achieve optimum proficiency in basic laparoscopic surgery [17], participating surgeons in the current study were required to have performed at least 30 laparoscopic cholecystectomies. Such a program was not available when earlier attempts to implement LAG were made, and a series reported by our instructing surgeon (M.F.) has revealed a high incidence of leakage (14%) and greater blood loss (239 mL) in his initial 43 patients [3]. Our results implied that skills acquired in these training sessions were actually transferable to the operative setting. As for the dry laboratory training mandated in the current study, the box trainer and VR simulators were used to achieve basic laparoscopic surgical competence and were not specific for LAG. Some of the components were not considered compulsory for surgeons who already had sufficient experience with laparoscopic cholecystectomy. Nevertheless, suturing technique is considered a mandatory skill needed to acquire the Endoscopic Surgical Skill Qualification organized by the Japan Society for Endoscopic Surgery, an ultimate goal of the surgeons who participated in this study. The two surgeons (Y.M. and S.I.) trained in the current study successfully acquired the Endoscopic Surgical Skill Qualification as of 2011, and participation in the dry laboratory training was helpful in that aspect.

Concerning the oncologic safety of the laparoscopic approach to gastric carcinoma, the mean number of lymph nodes retrieved from resected specimens was compatible with several series of LAG (Table 3), and fulfilled the minimal number required to evaluate pN in the TNM classification [24]. Furthermore, no port-site metastasis or recurrent disease was observed after a median follow-up period of 38.8 months. These findings, along with other studies, suggest that the laparoscopic approach is oncologically feasible for the treatment of early gastric carcinoma. Further evidence in this aspect will have to wait for the results of randomized phase III trials; we were allowed to participate in those trials due to the efforts described in the current study.

Since laparoscopic surgery for gastric cancer is considered a technically complex procedure, the learning curve period could be prolonged. Several previous reports have suggested that LAG with lymph-node dissection may require at least 50–90 cases for a surgeon to gain competence [25–27]. It was reported that complications frequently occur during the introductory period, where the greatest of precaution must be taken [3, 28]. In the current study, blood loss was the only parameter that showed a significant difference between the first and last 25 cases. In other words, the operating time did not significantly shorten during the same period. The operating time in the current series is comparable to those for other reported series (Table 3), however, so it may be that the plateau was attained more rapidly. More importantly, the current study clearly showed that surgeons who were trained adequately in open gastrectomy were capable of achieving acceptable short-term outcomes, even during the initial phase, if sufficient preparation was performed and instructions from a surgeon with the Endoscopic Surgical Skill Qualification were available.

There have been several studies from established laparoscopic surgeons comparing the short-term outcome of LAG with that of conventional open gastrectomy. In a randomized trial, Huscher et al. [21] reported mortality and

morbidity rates of 3.3 and 26.7% for LAG, which were equivalent to those for open gastrectomy. Other studies have also reported that morbidity rates associated with LAG are as low as those found for conventional open gastrectomies [29, 30]. The mortality and morbidity rates in the current study were 0 and 4%, respectively, and less than those observed in our historical series of open surgeries. They were at least comparable with those in a series of LAGs reported from other expert institutions (Table 3), demonstrating the adequacy of our method of implementing the new technique. We have had only one major surgical complication, an intra-abdominal abscess, but this was also handled conservatively.

We encountered one other intra-operative complication that was peculiar to the laparoscopic approach: a mesenteric injury due to disorientation resulting in a partial colectomy. However, by converting to open surgery, we were able to successfully complete the gastrectomy, and there were no further complications. In general, higher complication rates have been noted in patients that required conversions during laparoscopic cholecystectomy, appendectomy and colectomy as compared to the open approach [31–34]. However, Slim et al. [35] found that while the conversion generally resulted in an inferior outcome compared to that reported for open colorectal surgery, none of the patients who underwent a conversion at an early stage experienced a complicated postoperative course. Their findings conclusively demonstrate that an early decision to abandon the laparoscopic approach is the key to avoiding serious adverse events. Though our conversion rate was 6% and was higher than that observed in previous reports (Table 3), there were no serious consequences in our converted cases. Unnecessarily prolonged operating time was also avoided, as shown by the lack of a significant difference between the laparoscopy-only and conversion groups. Adequately judged and timely abandonment of the laparoscopic approach could therefore be considered part of a well-conducted surgery rather than a surgical failure.

To conclude, an adequate training program, including site visits by expert surgeons, in conjunction with established basic laparoscopy skills and a solid background in open gastrectomy from the perspective of the trainees are currently tkey to successfully and safely implementing LAG. It is not possible at this time to show whether LAG is oncologically feasible. The results of phase III trials comparing open surgery and LAG for early-stage gastric cancer by the Korean and Japanese study groups will ultimately answer this issue.

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EDITORIAL

Introduction of laparoscopy-assisted distal gastrectomy: a tale of two cities

Yasuhiro Kodera

The most frequent type of surgery for gastric cancer in Japan is distal gastrectomy, due to the predominantly distal origin of the tumors and the relatively early stages at which they are diagnosed. As it is technically less challenging than total gastrectomy, an increasing number of surgeons are currently in the process of adding laparoscopy-assisted distal gastrectomy (LADG) to their armamentarium. Not long ago, there were only a handful of surgeons that spoke on this subject at domestic surgical meetings. These surgeons attempted LADG with instruments and scopes that were not as sophisticated as the devices we have today. It is advisable, nowadays, to use the best devices and instruments available, and—even more importantly—to seek assistance and advice from an experienced laparoscopic surgeon when performing the LADG as a beginner. That brings us to the question of who taught these "first-generation" laparoscopic surgeons when they were beginners. The reality is that these highly-motivated "beginners" took the risk of creating a completely new type of surgery, assisted by less capable colleagues, using suboptimal devices, and with no one to seek for advice. There could have been casualties, due to either surgical complications or oncologically inadequate manipulation, and one can easily imagine that not all of these pioneers achieved the goal they wanted. It is important to note that those who were successful in their early attempts at LADG had all been (and still are) tremendously skillful at open surgery, with supreme knowledge of anatomy and meticulous surgical technique. In addition, they probably felt comfortable when they performed laparoscopic cholecystectomy for the first time, and may have had an instinct that they could perform more complex surgical procedures using this new approach.

By the first decade of the twenty-first century, a substantial proportion of the videos featuring gastric cancer surgery at domestic surgical meetings were performed by a laparoscopic approach. Unlike the "first generation" surgeons, younger experts in this field must have had a greater chance of interacting with or learning from more experienced surgeons. Thus, aside from welcoming an established laparoscopic surgeon as a new staff member, there were other ways of introducing the new approach to a surgical team with no prior experience of LADG.

More recently, two leading cancer centers in Japan, one in Nagoya and another in Yokohama, introduced LADG through a multistep training system planned by the staff surgeons of each institution and conducted after the approval of the corresponding institutional review board. Mochizuki et al. [1] described their experience at Aichi Cancer Center, Nagoya, in a recent issue of the journal *Gastric Cancer*. Two staff surgeons who were board-certified by the Japan Surgical Society, who had performed at least 50 open gastrectomies with lymph node dissection, and who had experienced >30 laparoscopic cholecystectomies during their careers as general surgeons participated in this program as trainees. They had some training both in the dry laboratory and with porcine models, and visited Nagoya University to observe LADG operated by Dr. Fujiwara, one of the "first-generation" laparoscopic surgeons [2]. The initial 10 LADGs at Aichi Cancer Center were then performed with either of the two surgeons as an operator and Dr. Fujiwara as an assistant, while the other

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surgeon handled the laparoscope to share the experience. After the initial 10 cases, the two surgeons performed a further 50 cases together, with one surgeon invariably taking the role of assistant while the other was operating. The morbidity rate during the training period was 2 %, and there was no mortality. Three cases were converted to open surgery, one due to injury of the mesocolon and the other two due to oncological reasons. More blood loss occurred in the earlier 25 cases, but no significant differences in other parameters were observed between the earlier and later groups.

In the Yokohama district, three surgeons at three independent hospitals, including Kanagawa Cancer Center, became trainees at their institutions in another training program featured in the current issue of *Gastric Cancer* [3]. Each surgeon sought assistance from another "first-generation" laparoscopic surgeon, but on this occasion only for the first three cases. Prior to this challenging experience, the three surgeons had performed >300 open gastrectomies, >100 laparoscopic cholecystectomies, >5 laparoscopic colectomies, and >5 laparoscopic wedge resections of the stomach. They also had some training in both the dry and wet laboratories, but—more importantly—they took substantial time to scrutinize and learn from the videos of exemplarily conducted LADGs. This, Dr. Yoshikawa et al. considers, was a key component of the training that may have been lacking from the Nagoya experience. With that much experience, and after that much effort, the authors declared that LADG was only a few steps away from open gastrectomy. Indeed, it is important to check the video after surgery to see which part of the surgery fell short of being ideally conducted.

On the other hand, profound knowledge of the surgical procedures per se does not guarantee that LADG can be conducted safely. Surgeons must be trained to handle the instruments with sufficient accuracy and dexterity, a task that usually cannot be achieved without moving their own hands. Training sessions with a dry box, virtual simulators, and live animals are therefore mandatory. Even with costly virtual reality simulators, it remains unclear whether an improvement in hand-eye coordination, as quantitated by the device, really does translate into success in a surgery as complex as LADG [4]. However, the transfer validity of these simulators is likely to improve as a response to increasing demand in the market. This editor is rather unsatisfied that the amount of training that should be assigned to the trainees in this aspect was not clearly defined in either the Nagoya or the Yokohama experience. Perhaps the amount of training needed to acquire the necessary skills depends on the inherent ability of the trainees and therefore cannot be defined. At the same time, one must be realistic regarding the time and cost that can be expended on such training, given that the trainees in both projects were, at the same time, full-time staff surgeons of prominent hospitals. The three surgeons in Yokohama seemed to be comfortable with performing LADG after only three site visits by the experts. This editor is left with amazement—along with some skepticism—that they may have been so exceptionally talented. A great deal of time, effort, and cost would be required to train a less talented trainee; whether such a trainee could be identified quantitatively using simulators and then discouraged from pursuing a career as a surgeon are important issues for future debate.

Both Dr. Mochizuki and Dr. Yoshikawa were subsequently qualified by the Japan Society for Endoscopic Surgery as instructing surgeons in this field after scrutiny of their unedited videos through a stringent review system. Not many surgeons have had such glory and, with this tremendous outcome, the experiences at Nagoya and Yokohama can both be considered successes. Can such training programs be provided for all Japanese institutions? One advantage the colleagues at the two cancer centers had over other general surgeons was that they belonged to celebrated high-volume hospitals as staff members. Even if they selected patients strictly in terms of body mass index and other factors that may influence the short-term outcome of LADG, they did not have to wait long for the next opportunity after each fruitful experience. This advantage would apply even more prominently to institutions in Korea, where most patients with gastric cancer are treated at super-high-volume centers that conduct >1000 gastrectomies per a year. When the results of various on-going phase III trials are found to be positive [5, 6], it would be much easier in South Korea than in other countries to declare formally (in the guidelines, for instance) that LADG is the standard of care. In Japan, an increasing number of young surgeons are now being trained in some high-volume training centers with their own training programs [7, 8]. Institutions that fail to employ graduates of these highly regarded programs should do their best to follow the steps of Drs. Mochizuki and Yoshikawa and attempt to convert an expert in open surgery into a capable laparoscopic surgeon.

The day will eventually come when the first gastric cancer surgery in a young surgeon's career needs to be performed by the laparoscopic approach. Is it possible that the many years we spent as residents learning to perform open surgery will be simply dismissed as unnecessary for the younger generation? It is painful to answer in the affirmative, but we must move forward. We should perhaps remember how, several decades ago, we suffered as a second assistant aiding a senior surgeon in a low anterior resection. With a retractor in each hand, we stood between the thighs of a patient for several hours to ensure that the operator and his first assistant could proceed with their