Clinical evaluation of laparoscopy-assisted distal gastrectomy for early gastric cancer

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ABSTRACT

Recently, laparoscopic surgery has gained rapid acceptance on clinical grounds, and its range of application has expanded. Since laparoscopy-assisted distal gastrectomy (LADG) was first reported in 1994, most gastrointestinal surgeons have become highly interested in this surgical procedure for early gastric cancer. To evaluate short-term surgical validity in patients with early gastric cancer located in the middle or lower part of the stomach, surgical outcome of the LADG with extraperigastric lymph node dissection was compared with open distal gastrectomy (ODG). Between October 2000 and November 2004, LADG with lymph node dissection was performed on 44 patients, and ODG on 59. There were no statistical differences between the two groups in sex, age, body mass index (BMI), and concurrent illness. The mean operation time was 246±42 min in the LADG group and 253±46 min in the ODG group, but the amount of blood loss (125±101 g) in the LADG group was significantly less than that (243±128 g) in the ODG group. The results of pathological findings of resected specimens showed no differences between these groups in terms of the number of lymph nodes retrieved. Postoperative recovery was faster in the LADG group than in the ODG group, as reflected by a shorter hospital stay (19.9±8.2 vs 24.8±6.8: $p<0.05$). There were no operative deaths or hospital deaths in any of the patients. Laparoscopic surgery is currently the gold standard because it is a minimally invasive procedure, less painful, and it allows quicker recoveries. Our results confirmed

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that LADG accompanied with either D1 + α or D1 + β lymph node dissection is appropriate in terms of safety and as a cure. LADG is recommended as a preferable alternative to ODG for patients with early gastric cancer.

Key words : Laparoscopy-assisted distal gastrectomy, Gastric cancer, Lymph node

INTRODUCTION

Gastric cancer is one of the most common malignancies and widely prevalent in Japan[1, 2]. The incidence of early gastric cancer has increased because of the development of diagnostic techniques such as endoscopy, biopsy, endoscopic ultrasonography[3], and mandatory mass examination for gastric cancer. Patients with gastric mucosal cancer, well or moderately differentiated adenocarcinoma, cancer of 2cm diameter or less, and cancer without ulcer or ulcer scar, are good candidates for endoscopic mucosal resection (EMR) because it is the least invasive management and lymph node metastasis is extremely rare in this type of gastric cancer. However, in cases of gastric mucosal cancer that are not eligible for the forementioned EMR or in case of submucosal cancer, adequate gastrectomy and perigastric lymph node dissection with possible metastasis should be performed[4]. Since the clinical benefits of laparoscopic cholecystectomy were first reported[5, 6], laparoscopic surgery has been considered to be less invasive than conventional open surgery, and has now been adopted for the gastrointestinal diseases[7, 8]. Laparoscopy-assisted distal gastrectomy(LADG), was first reported by Kitano et al. in 1994[9] and most of gastrointestinal surgeons have become highly interested in this surgical procedure for early gastric cancer.

Several investigators reported that LADG offered clinical advantages, including less operative blood loss, less pain, earlier recovery of bowel activity, earlier resumption of oral intake, and a shorter hospital stay, when compared with the conventional open surgery[9-12]. However, the safety and efficacy of LADG for early gastric cancer still remains controversial.

Herein, we reported the surgical outcome of the LADG with extraperigastric lymph node dissection compared with open distal gastrectomy (ODG) in patients with early gastric cancer located in the middle or lower part of the stomach and evaluate its short-term surgical validity.

MATERIALS AND METHODS

Eligible Patients

Between October 2000 and November 2004, LADG with lymph node dissection was performed on 44 patients with early gastric cancer located in the middle or lower part of the stomach in the First Department of Surgery, Sapporo Medical University School of Medicine and Department of Surgery, Municipal Muroran General Hospital. One hundred and three patients with early gastric cancer received radical distal gastrectomy, while ODG was performed on 59 patients. Preoperatively, we gave an appropriate explanation about LADG and ODG, and written informed consent obtained from all patients who agree to be treated by operative procedure. Patients who had been preoperatively diagnosed as having histologically-proven T1, N0 gastric cancer (invasion to the mucosa or submucosa with no apparent lymph node involvement) were eligible for this study. These are the terms defined in the current version of the Japanese Classification of Gastric Carcinoma[13]. The preoperative staging evaluation regarding T and N categories were routinely-performed by expert gastroenterologists and radiologists with combined modalities consisting of barium contrast studies, endoscopy, endoscopic ultrasound, and computerized tomography. The patients who had been consulted for salvage surgery after failure to achieve complete resection through endoscopoic mucosal resection

(EMR) and endoscopic submucosal dissection (ESD), were also considered eligible for LADG.

Lymphadenectomy

LADG and ODG were accompanied with either D1 + α or D1 + β lymph node dissection, as defined in the terms of the Japanese Classification of Gastric Carcinoma[13] and in the first and revised version of Gastric Cancer Treatment Guidelines[14]. D1 + α dissection denotes co-resection of perigastric lymph nodes (lymph node No. 1, 3, 4sb, 4d, 5 and 6) and lymph nodes at the base of the left gastric artery (No. 7), and D1 + β denotes additional dissection of lymph nodes along the anterosuperior group of the common hepatic artery (No. 8a) and around the celiac artery (No. 9). D1 + α was performed for the patients with preoperative diagnosis of mucosal cancer, and D1 + β was performed for the patients with preoperative diagnosis of submucosal cancer. There was no difference in strategy for lymph node dissection between LADG and ODG.

Laparoscopic Technique

LADG was performed by experienced surgeons according to a standard technique reported by Adachi et al.[11] and Kitano et al.[15] The operation was carried out under general anesthesia and epidural anesthesia with preoperative bowel preparation and intra-operative antibiotic cover. The patient wore graduated compression stockings, and intermittent pneumatic-compression boots were applied to the lower extremities just after entry into the operating room. Laparoscopic surgery was done with the patient in the supine position under CO^2 pneumoperitoneum of 8-10 mm Hg through the subumbilical trocar inserted via the open method. Through this first port, a laparoscope

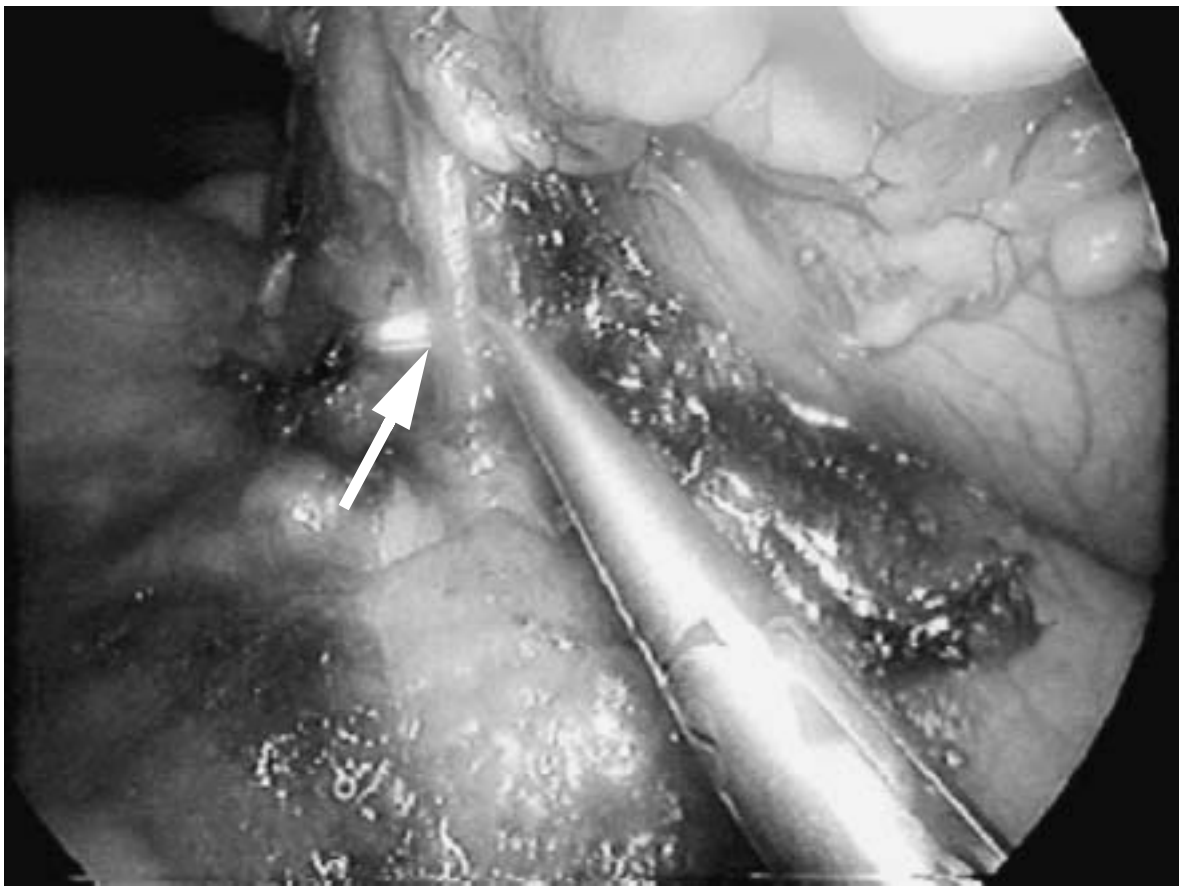

Fig. 1 The dissection of the lymph nodes (No. 6) along the right gastroepiploic artery. The right gastroepiploic veins and arteries were identified and divided at the lower edge of the pancreas head. An arrow shows the right gastroepiploic vein.

(Olympus, Tokyo, Japan) was introduced into the abdominal cavity, and additional four surgical ports were placed bilaterally (one 10mm and one 5mm port on each side). First the greater omentum was divided between the large curvature of the stomach and the transverse colon, and omental branches from the gastroepiploic vessels were coagulated using laparoscopic coagulating shears (Harmonic Scarpel, Ethicon Endo-Surgery, Cincinnati, OH). Subsequently, the left gastroepiploic artery and vein were isolated and cut near the splenic flexure of the colon. The right gastroepiploic veins and arteries were then identified and divided at the lower edge of the pancreas head after double clipping for the dissection of the lymph node (No. 6) along the greater curvature (Fig. 1). Then the infrapyloric artery was divided to expose the duodenum. After the lesser omentum was opened, the right gastric artery was divided at its origin by double clips in the hepatoduodenal ligament. Then the left gastric vein was exposed at the base of the common hepatic artery and the splenic artery, and divided using clips and coagulating shears. As a result, the common hepatic artery was exposed and No. 8a lymph nodes were dissected in case of D1+β lymph node dissection. The left cardiac and super gastric lymph nodes toward the cardiac lesion were dissected down to the distal portion of the stomach. A midline skin incision of 4–6 cm in length at the epigastrium under the xiphoid. The duodenum was transected 1cm distal to the pyloric ring by an endoscopic staplar (Endo cutter 60; Ethicon, Cincinnati, OH). After exteriorization of the distal stomach extra-abdominally though the midline skin incision, a 100 mm staplar (linear stapler GIA USSC, Norwalk, CT) was applied at the greater curvature of the stomach, and the resected stomach was removed, together with the lymph nodes. To confirm the sufficiency of resection margin, macroscopic inspection of the resected specimen was done in at the operating theater immediately following resection, and pathologic examination of the resection margin was routinely-performed with a frozen section. Accordingly, a Billroth I anastomosis was performed by handsewing through the same incision (Fig. 2).

After the laparoscopic surgery, dissected lymph nodes were divided from the resected stomach according to the current version of the

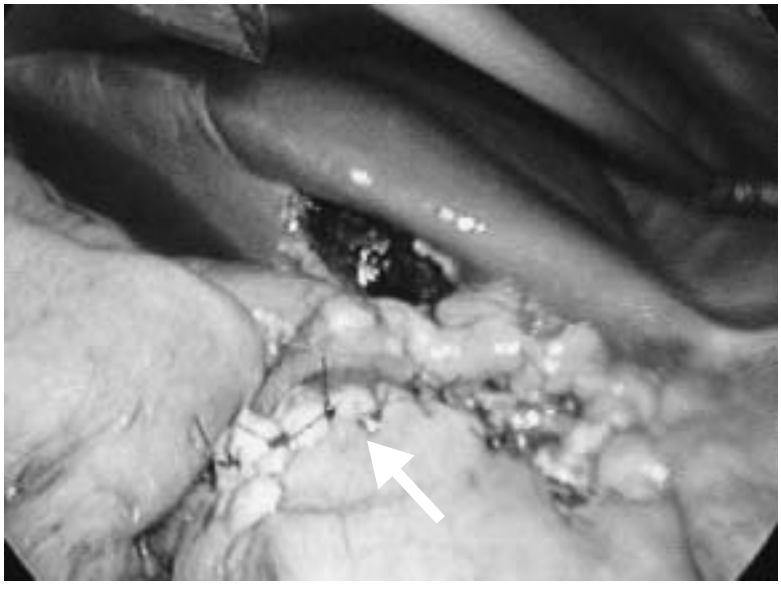

Fig. 2 Laparoscopic view after a Billroth I anastomosis. Gastrojejunostomy was performed by handsewing through a midline skin incision under the xiphoid. An arrow shows the suture line of gastrojejunostomy.

Japanese Classification of Gastric Carcinoma[13].

Postoperative Examinations

Resected spiecimens were fixed in formalin and hematoxylin and eosin stainings were performed for pathologic evaluation of the depth of cancer invasion, the number of lymph node metastasis, and for conclusive stage classification. The age and sex of the patients were documented, and the following features were obtained from medical records: histological type, depth of wall invasion, tumor size, presence of lymph node metastasis, and co-morbidity. Surgical details included the operative time, estimated blood loss, length of postoperative hospital stay, surgical complications, and early and long-term outcome variables were also documented, as were postoperative complications included anastomotic bleeding, anastomotic leakage, anastomotic stenosis, wound infection, gastric stasis, pneumonia and intestinal obstruction.

Statistical Analysis

Student t-test was used to compare parametric variables such as operation time, while Mann-Whitney U-test was used to compare non-parametric variables such as postoperative hospital stay. A two-tailed probability of less than 5% (p <0.05) was considered significant.

RESULTS

During four years, LADG or ODG were performed on 44 and 59 patients with early gastric cancer, respectively. Intraoperatively, conversion to a open procedure was required in only one patient due to the difficulty in gaining a comfortable and safe visual field for operation, due to excessive intraabdominal fat. Table 1 shows the clinicopathological characteristics of patients receiving LADG or ODG. There were no statistical differences between the groups in sex, age, body mass index (BMI), and concurrent illness. Moreover, there were no significant differences in depth of cancer invasion or types of tumor differentiation for preoperative diagnosis. On the other hand, tumor size (33±18 mm) of the ODG group was greater than that (24±13 mm) of the LADG group. The mean operation time was 246±42 min (range: 174-348) in the LADG group and 253±46 min (range: 184-353) in the ODG group, but the amount of blood loss (125±101g) of the LADG group was significantly less than that (243±128 g) of the ODG group (Table 2). Preoperative diagnosis of depth

Table 1 Clinicopathological characteristics

Characteristics	LADG (n=44)	ODG (n=59)	p value
Sex (male/female)	28/16	36/23	NS
Age (year)	62±11	67±12	NS
BMI	24±2	24±2	NS
Concurrent illness			NS
Hypertension	6	6	
Diabetes mellitus	2	5	
Ischemic heart disease	2	4	
Depth of invasion			NS
M	28	27	
SM	16	32	
Tumor size (mm)	24±13	33±18	<0.05
Tumor differentiation			NS
Differentiated	30	31	
Undifferentiated	14	28	

LADG, laparoscopy-assisted distal gastrectomy; ODG, open distal gastrectomy; BMI, body mass index; M, mucosa; SM, submucosa; NS, not significant; values are mean ± standard deviations.

Table 2 Operative and pathological findings

Characteristics	LADG (n=44)	ODG (n=59)	*p* value
Operation time (minutes)	246 ± 42	253 ± 46	NS
Blood loss (g)	125 ± 101	243 ± 128	<0.001
Depth of invasion			NS
m	25	24	
sm1	7	17	
sm2	8	15	
mp	4	3	
Number of lymph nodes retrieved	28 ± 15	32 ± 14	NS
Lymph node metastasis			NS
n0	40	51	
n1	4	7	
n2	0	1	

LADG, laparoscopy-assisted distal gastrectomy; ODG, open distal gastrectomy; m, mucosa; sm, submucosa; mp, muscularis propria; ss, subserosa; n0, negative; n1, metastases to group 1 lymph nodes; n2, metastases to group 2 lymph nodes; NS, not significant; values are mean ± standard deviations.

of cancer invasion was mucosa in 55 patients and submucosa in 48. The actual depth as comfirmed by postoperative pathological findings was mucosa in 49 patients, submucosa in 47, and muscularis propria in 7. Preoperative underestimation of the depth of cancer invasion occurred in 7 patients (15.9%) who received LADG and 8 patients (13.6%) who received ODG. The results of pathological findings of resected specimens revealed no differences between these groups in terms of the number of lymph nodes retrieved. Lymph node metastases were observed in 4 and 8 patients of the LADG and ODG group respectively.

Table 3 shows the postoperative outcomes for the two groups. Even though there were no significant differences in time to first walking and oral feeding between the two groups, postoperative recovery was faster in the LADG group than in the ODG group, as reflected by a shorter hospital stay (19.9 ± 8.2 vs 24.8 ± 6.8: $p < 0.05$). In addition, the leukocyte count in the LADG group was lower ($9.6 \pm 2.9 \times 10^3$μl vs $12.7 \pm 2.6 \times 10^3$μl: $p < 0.05$) on day one than that in the ODG group.

There were no operative deaths or hospital deaths in any of the patients. In the LADG group, postoperative complications were ob-

Table 3 Postoperative outcomes

Characteristics	LADG (n=44)	ODG (n=59)	*p* value
First walking (POD)	2.0 ± 0.2	2.4 ± 0.5	NS
First water drinking (POD)	2.8 ± 1.6	4.7 ± 0.7	<0.005
First oral feeding (POD)	5.6 ± 2.7	6.1 ± 1.6	NS
Leukocyte (103/μl)			
POD1	9.6 ± 2.9	12.7 ± 2.6	<0.05
POD3	8.4 ± 2.9	9.8 ± 3.1	NS
POD7	7.1 ± 2.1	7.7 ± 2.7	NS
Postoperative hospital stay (days)	19.9 ± 8.2	24.8 ± 6.8	<0.05

LADG, laparoscopy-assisted distal gastrectomy; ODG, open distal gastrectomy; NS, not significant; values are mean ± standard deviations; POD postoperative day.

Table 4 Postoperative morbidities and mortalities

Characteristics	LADG (n=44)	ODG (n=59)	*p* value
Anastomotic bleeding	0	1	NS
Anastomotic leakage	1	1	NS
Anastomotic stenosis	2	2	NS
Wound infection	0	3	NS
Gastric stasis	2	2	NS
Pneumonia	0	1	NS
Intestinal obstruction	0	1	NS
Death in hospital	0	0	NS

LADG, laparoscopy-assisted distal gastrectomy; ODG, open distal gastrectomy; NS, not significant; values are mean ± standard deviations; POD postoperative day.

served in 5 patients (11.4%) and consisted of one case of minor anastomotic leakage, and two cases of anastomotic stenosis, two cases of gastric stasis. On the other hand, postoperative complications were observed in 11 patients (18.6%) and consisted of one case of anastomotic bleeding, one case of minor anastomotic leakage, two cases of anastomotic stenosis, three cases of wound infection, two cases of gastric stasis, one case of pneumonia, and one case of intestinal obstruction (Table 4).

Postoperatively, one patient had liver metastases in the LADG group and two patients died of cardiac infarction and intracranial bleeding in ODG. No recurrence has occurred in the other patients, who have been followed up postoperatively for a median interval of 669 days.

DISCUSSION

Recently, laparoscopic surgery has gained rapid acceptance on clinical grounds, and its range of application has expanded. Progress in laparoscopic procedures for abdominal organs has been achieved, and this minimally invasive surgery is now enthusiastically applied for surgery in other organs. It's a well-known fact that the number of LADGs employed for early gastric cancer located in the middle or lower part of the stomach is increasing worldwide. Currently, LADG is still defined as being the subject of clinical research, as defined by Gastric cancer treatment guidelines in Japan. Although several studies have reported clinical benefits of LADG, these trials have been uncontrolled, non-randomized controlled studies. LADG remains controversial in terms of its safety and efficacy, and this surgical procedure is also considered to be technically more complicated than the open method[16].

The number of lymph nodes found in resected specimen is related to the radicality of an operation. All of the LADG procedures accompanied with either D1 + α or D1 + β lymph node dissection were successfully performed using laparoscopy, with the exception of in one obese patient. There are several retrospective studies on the curability rate associated with LADG which have focused on the number of lymph nodes retrieved between LADG and ODG[17, 18]. These studies showed that there was no significant difference in the number retrieved between LADG and ODG. Likewise, there was no statistical difference in the overall mean number of lymph nodes retrieved between the two groups in our study (28±15 vs 32±14: NS). Although lymph node metastases were observed in 12 patients, all patients were carefully followed and are still alive. In this regard, LADG is not inferior to ODG in terms of its radicalness. Histological analysis revealed 4 patients with advanced gastric cancer in the LADG group, and 3 in the ODG group. Conclusive clinical stages of the patients were Stage IA in 88 patients, Stage IB in 11 patients, and Stage II in 4 patients. The preoperative diagnosis regarding T categories was fairly accurate,

but the depths of invasion were found to be underestimated in 14.6% (15/103) patients. To extend the indication of LADG to T2 stage gastric cancer, largescale phase II and phase III studies are needed in the future.

In the present study, we found that the LADG group had significantly less blood loss (125 ± 101 g vs 243 ± 128 g: $p < 0.001$) and shorter postoperative hospital stay (19.9 ± 8.2 vs 24.8 ± 6.8: $p < 0.05$), although the mean operation time was the same. Furthermore, we have observed that the leukocyte count in the LADG group on day one was lower than that in the ODG group ($9.6 \pm 2.9 \times 10^3 \mu$lvs$12.7 \pm 2.6 \times 10^3 \mu$l: $p < 0.05$). These findings may support the idea laparoscopic surgery offers several perioperative benefits including a lower inflammatory response and less stress during surgery. A relation between laparoscopic surgery and fewer immunological changes after surgery has been reported[19, 20]. By examination of post surgical immunological respose, Fujii et al.[21] found that the host defense is less depressed, as assessed by natural killer cell cytotoxicity, neuroendocrine response and T lymphocytes. Moreover, the production of INF-gamma as Th1 cell function decreased significantly on the third postoperative day after ODG but increased after LADG, and the production of IL-4, representing Th2 cell function, increased postoperatively after ODG but not after LADG. Changes in T lymphocyte subsets after surgery may be associated with the degree of surgical stress, including the demands of minilaparotomy, operation time, and operative blood loss. In this study, the size of wound was very small in LADG (data not shown). Consequently, these findings indicated that the Th1/Th2 balance is less impaired by laparoscopic surgery than by the conventional open surgery.

In conclusion, laparoscopic surgery is currently the gold standard because it is a minimally invasive procedure, less painful, and affords quicker recovery. Patients can return to normal activities without a significant loss in their quality of life. Our results confirmed that LADG accompanied with either D1 + α or D1 + β lymph node dissection was feasible in terms of safety and its efficacy as a cure. LADG is recommended as a preferred alternative for patients with early gastric cancer.

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