Surg Endosc (2008) 22:2003–2008
DOI 10.1007/s00464-008-0016-8

Functional evaluation after vagus nerve–sparing laparoscopically assisted distal gastrectomy

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Received: 9 April 2008 / Accepted: 20 May 2008 / Published online: 2 July 2008

Abstract
Background Vagus nerve–sparing laparoscopically assisted distal gastrectomy (Vs-LADG) for early gastric cancer has been introduced to reduce postgastrectomy syndrome, but its clinical and functional outcomes remain unclear.
Methods Of the 105 patients reviewed in this study, 75 underwent Vs-LADG and 30 underwent laparoscopically assisted distal gastrectomy (LADG) for gastric cancer between January 1999 and May 2006. The clinical and functional outcomes of these two groups were compared.
Results The clinical and pathologic background between the two groups did not differ. The incidence of gallstone was significantly lower in the Vs-LADG group than in the LADG group ($p < 0.05$), but no differences existed in duration of surgery, intraoperative blood loss, number of retrieved lymph nodes, time to first flatus after surgery, or length of hospital stay between the two groups.
Conclusions As shown by the findings, Vs-LADG is a safe and minimally invasive surgery that may decrease the incidence of gallstone formation after gastrectomy.

Keywords Early gastric cancer · Functional evaluation · Laparoscopic surgery · Nerve sparing · Vagus nerve

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Gastric cancer is one of the most common malignant diseases in Japan, and the incidence of early gastric cancer (EGC) has increased to more than 50% of the gastric cancers diagnosed. This increased incidence of EGC may be due to the development of higher quality endoscopic instruments, improved detection of EGC, and prevalence of mass screening and individual checkups [1, 2].

The prognosis of patients with EGC is known to be excellent, with 5-year survival rates exceeding 90% [3, 4]. The focus of interest in the treatment of EGC has shifted to minimally invasive treatments and improvement in the quality of life after gastrectomy without impairment to the excellent prognosis. Several minimally invasive treatments recently introduced include endoscopic mucosal resection [5], endoscopic submucosal dissection [6], laparoscopic surgery [7, 8], and limited resection by open surgery [9, 10].

Vagus nerve preservation combined with gastrectomy in open surgery, introduced in 1991, was expected to decrease postgastrectomy syndrome [11]. With this procedure, the hepatic branches of the anterior vagal trunk that innervate the liver and biliary tract are preserved, as well as the celiac branches of the posterior vagal trunk that innervate the small intestine. However, the functional effect of this technique remains controversial.

Since the first report of laparoscopically assisted distal gastrectomy (LADG) in 1994, this procedure has been widely accepted as the surgical treatment for EGC in Japan. The number of patients undergoing LADG has been increasing rapidly [12] because LADG is considered to be safer and less invasive [13], and to result in less postoperative pain, earlier return of bowel function, shorter hospitalization [14], less postoperative disability, and better cosmetic results [15].

We previously reported the technique of vagus nerve–sparing LADG (Vs-LADG) [16], but functional evaluation after Vs-LADG had not yet been investigated. In this study, we evaluated the clinical and functional outcomes of Vs-LADG compared with those of LADG.

Methods

The anatomic distributions of the stomach's regional lymph nodes (LNs) are numbered in this article according to the Japanese Classification of Gastric Carcinoma, 2nd English edition [17].

Indications

The indications for Vs-LADG were depth of tumor invasion confined to the mucosal or submucosal layer (T1), no possible LN metastasis (N0), and tumor unsuitable for endoscopic mucosal resection, endoscopic submucosal dissection, or laparoscopic local resection. Tumor size and histologic type were not considered as indications.

Surgical procedure

The patient is placed in a reverse Trendelenburg position with the arms tucked at the sides and the legs abducted. The camera port is placed close to the umbilicus. Two ports are placed immediately lateral to the rectus muscle on either side, 3 cm cranial to the umbilicus. An additional two 5-mm ports are placed more medially, just caudal to the xiphoid process and 7 cm apart. Inferior ports 12 mm in width are placed to allow for insertion of stapling devices (Fig. 1).

After laparoscopic survey of the abdominal cavity, the greater omentum is divided along the transverse colon to the lower pole of the spleen using ultrasonic shears (laparoscopic coagulating shears [LCS]; Ethicon, Cincinnati, OH, USA). The left gastroepiploic vessels are cut with a LigaSure device (Valleylab, Tyco Healthcare, Norwalk, CT, USA).

The no. 4 sinistra below (sb) LNs are dissected by dividing the greater omentum with LCS. After division of the greater omentum at the pylorus, including the no. 4d LNs, attention must be paid to the inferior border of the pancreas head, which is the landmark for dissection of the no. 6 LNs. The roots of the right gastroepiploic vein and artery are exposed and cut with double clips, thereby dissecting the infrapyloric no. 6 LNs. Mobilization of the duodenum 3 cm distal to the pylorus is performed by LCS. The duodenum is transected distal to the pylorus with an endoscopic stapling device. The right gastric artery is exposed and divided at its origin with clips, resulting in dissection of the no. 5 LNs.

The lesser omentum is divided at the center toward the abdominal esophagus to remove the LNs along the lesser curvature that includes LN nos. 1 and 3, and to preserve the

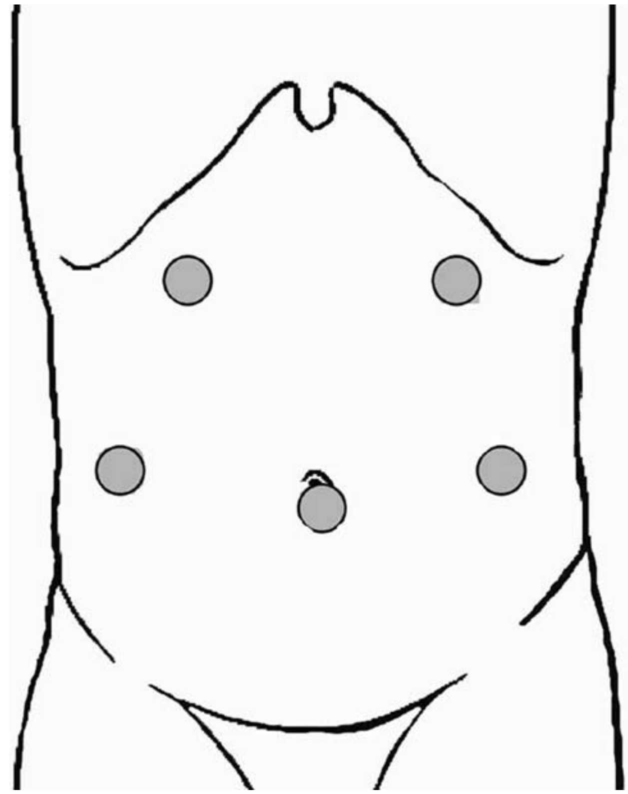

Fig. 1 Trocar placements. The initial trocar was placed at the infraumbilicus using the open technique. Four trocars were added at the upper abdominal portions

hepatic branch from the anterior vagal trunk. The hepatic branches running across the lesser omentum near the liver are found in a magnified view (Fig. 2).

Next, the posterior vagal trunk and celiac branches that run along the posterior wall of the abdominal esophagus

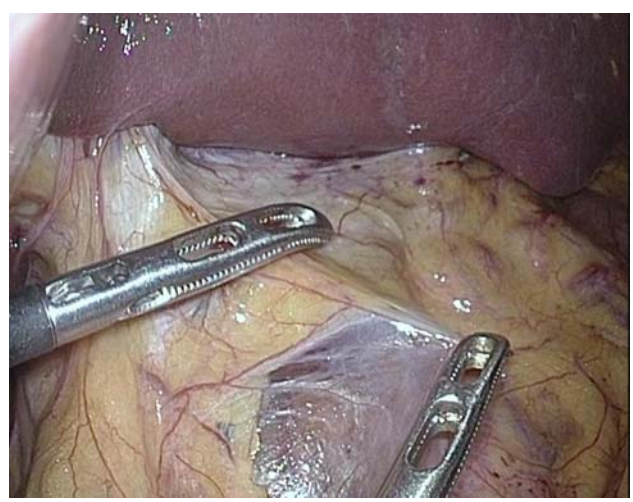

Fig. 2 Preservation of the hepatic branch of the vagus nerve. The lesser omentum was divided just below the hepatic branch to preserve this nerve

and to the celiac ganglion are identified. With exposure of diaphragm's right crus and the anterolaterodorsal side of the abdominal esophagus, the posterior vagal trunk is isolated and retracted toward the right side with a vessel loop.

After exposure of the common hepatic artery and gastropancreatic folds, the no. 8a LNs, located along the common hepatic artery, are dissected. In this step, the hepatic nerve plexus that runs along the common hepatic artery must be preserved. Nos. 9 and 11p LNs along the celiac artery and splenic artery are removed, and the left gastric artery and celiac axis are exposed. The celiac branches of the posterior vagal trunk run down along the lesser curvature to the celiac ganglion. After isolation of the celiac branches from the left gastric artery, the left gastric artery is divided with double clips (Fig. 3). The nerves of Latarget are divided from the celiac branches. Retraction of the celiac branches toward the right side facilitates this procedure. The vagus nerve–sparing LN dissection then is completed (Fig. 4). The stomach is transected using a minilaparotomy.

Before introducing Roux-en-Y reconstruction in March 2004, we had performed extracorporeal Billroth I anastomosis. If a tumor was located more orally, we preferred to perform Billroth II reconstruction with Braun anastomosis. Since March 2004, we have mainly performed Roux-en-Y gastrojejunostomy with stapled anastomosis, performed extracorporeally.

Patients

This study reviewed 105 patients with gastric cancer who underwent curative surgery between January 1999 and May 2006. The Vs-LADG procedure was performed for 75 patients and the LADG procedure for 30 patients. For T1 tumors, whether Vs-LADG or LADG was performed was decided by the operators considering the age and preference of patients after informed consent. We indicated Vs-LADG for all T1 gastric cancer patients younger than 75 years who agreed with nerve preservation surgery.

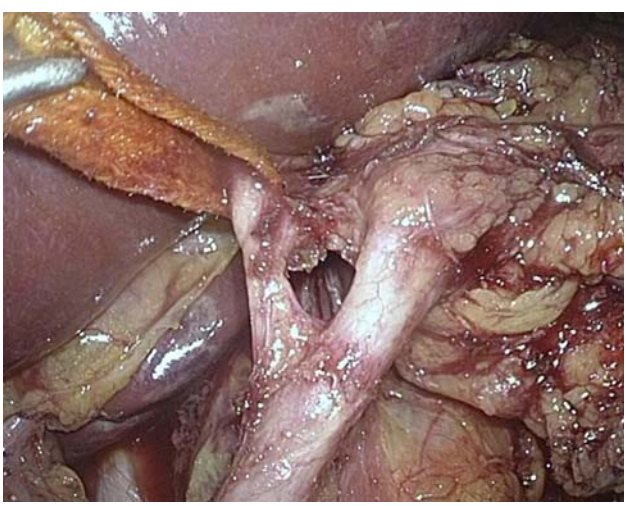

Fig. 3 Exposure of the junction of the celiac branch and the left gastric artery (LGA). The celiac branch runs to the celiac ganglion together with the LGA, and this branch was jointed to the LGA and positioned just behind this artery

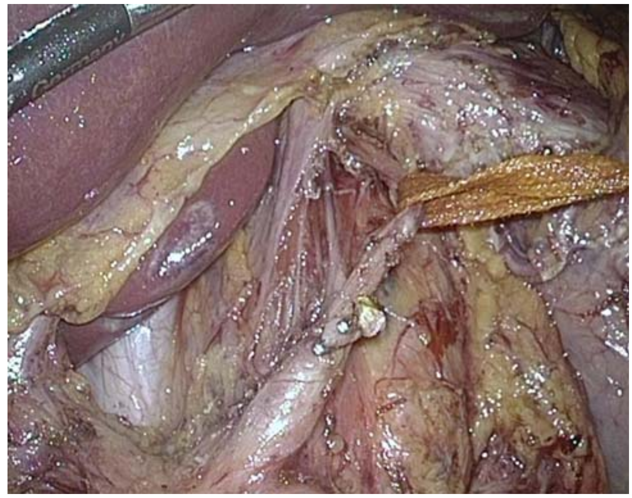

Fig. 4 Complete lymph node dissection with preservation of the celiac branch

For T2 tumors, LADG was applied. Preoperative survey was performed by abdominal ultrasonography. Patients who had undergone no preoperative abdominal ultrasonography were excluded from this study. In addition, patients with gallstone were excluded because they underwent cholecystectomy concurrently. Patients with a history of cholecystectomy or combined resection of other organs were excluded from this study.

Data were collected from operation and pathologic records. The following variables were evaluated: age, sex, body mass index (BMI), comorbidity, tumor location, tumor size, histologic type, depth of wall invasion, LN metastasis, pathologic stages; and surgical details including operating time, blood loss, scope of LN dissection, type of reconstruction, number of retrieved LNs, postoperative complications, time to first flatus, length of postoperative hospital stay, and follow-up period.

Functional evaluation

To evaluate the effect of nerve preservation, body weight (BW), food intake, symptoms, gallstone, hemoglobin, serum albumin, and serum cholesterol 1 year after surgery were compared with those before surgery. Body weight change was defined as the percentage of change in BW 1 year after surgery compared with the preoperative BW. Food intake change was self-evaluated by patients as a percentage of change in the volume of food intake 1 year after surgery compared with that before surgery.

The symptoms investigated included heartburn, diarrhea, constipation, and dumping syndrome. Gallstone was examined by abdominal ultrasonography.

Statistical analysis

The means and standard deviations of the collected data were calculated. Data values were statistically analyzed using Mann-Whitney *U* test, Student's *t*-test, and chi-square test using the Stat View 5.0 software package (SAS Institute, Cary, NC, USA). All results with *p* values less than 0.05 were considered statistically significant.

Results

The two groups did not differ in age, sex ratio, BMI, or concurrent diseases (Table 1). Tumors were significantly smaller in size and the adenocarcinoma better differentiated with Vs-LADG than with LADG (both $p < 0.05$) (Table 2). No differences in tumor location, depth of wall invasion, positive LN, or pathologic stages existed between the two groups. Dissection of D1 + α and D + β LNs was performed significantly more often in Vs-LADG than in LADG ($p < 0.05$). The two groups did not differ in terms of complications or number of retrieved LNs.

The time to first flatus tended to be shorter with Vs-LADG than with LADG (p = 0.062), whereas no differences were observed in other postoperative measurements between the two groups (Table 3). The incidence of gallstone was significantly lower with Vs-LADG than with LADG, but other variables of nutrition and symptoms showed no difference between the two groups (Table 4).

Table 1 Patient characteristics[a]

Characteristics	LADG (*n* = 30)	Vs-LADG (*n* = 75)	*p*-value
Age (years)	60.0 ± 13.0	61.9 ± 9.9	NS
Male/female	23/7	50/25	NS
BMI	22.2 ± 2.6	22.5 ± 2.7	NS
Concurrent disease			
Absent/present	20/10	50/25	NS
Cardiac angina	0	3	
Arterial hypertension	3	10	
Diabetes mellitus	2	6	
Hepatic	1	2	
Others	4	10	

LADG, laparoscopically assisted distal gastrectomy; Vs-LADG, vagus nerve–sparing laparoscopically assisted distal gastrectomy; NS, not significant; BMI, body mass index

[a] Data are given as the mean ± standard deviation or number

Table 2 Histopathologic findings[a]

Tumor	LADG (*n* = 30)	Vs-LADG (*n* = 75)	*p*-value
Location: middle/lower third	13/17	41/34	NS
Tumor size (mm)	41.1 ± 24	31.6 ± 18	<0.05
Histologic type: well/poorly differentiated	9/21	43/32	<0.05
Depth of wall invasion: m/sm/mp/ss/se	8/15/4/2/1	37/31/5/2/0	NS
Lymph node metastasis: absent/present	23/7	68/7	NS
Pathologic stage: Ia, Ib, II, IIIa[b]	19/8/2/1	63/9/3/0	NS

LADG, laparoscopically assisted distal gastrectomy; Vs-LADG, vagus nerve–sparing laparoscopically assisted distal gastrectomy; NS, not significant; m, mucosa; sm, submucosa; mp, muscularis propria; ss, subserosa; and se, serosa

[a] Data are given as the mean ± standard deviation or number

[b] From the Classification of the Japanese Gastric Cancer Association

Table 3 Postoperative course and complications[a]

Factors	LADG (*n* = 30)	Vs-LADG (*n* = 75)	*p*-value
Operative findings			
Operation time (min)	292 ± 59	270 ± 52	NS
Blood loss (g)	100 ± 97	88 ± 92	NS
Scope of LN dissection[a]			
D1 + α/D1 + β/D2[b]	2/16/12	8/59/8	<0.05
Reconstruction			
B-I/B-II/R-Y[c]	8/3/19	34/5/36	NS
No. of retrieved LNs	31.1 ± 13.3	32.4 ± 12.5	NS
Postoperative complications			
No. of patients with complications: *n* (%)	5 (17)	11 (14.7)	NS
Pancreatic injury	1	2	
Anastomotic leakage	1	0	
Anastomotic stenosis	0	3	
Anastomotic bleeding	0	1	
Abdominal abscess	1	3	
Others	2	2	
Postoperative course			
First flatus (days)	3.1 ± 0.6	2.7 ± 0.8	0.062
Postoperative hospital stay (days)	11.2 ± 8.6	10.7 ± 6.7	NS
Follow-up period (mo)	37.2 ± 20.1	42.1 ± 17.6	NS

LADG, laparoscopically assisted distal gastrectomy; Vs-LADG, vagus nerve–sparing laparoscopically assisted distal gastrectomy; NS, not significant; LN, lymph node

[a] Data are given as the mean ± standard deviation or number

[b] α indicates no. 7; β indicates nos. 7, 8a, and 9

[c] B-I indicates Billroth-I; B-II indicates Billroth-II; and R-Y indicates Roux-en-Y

Table 4 Nutrition and symptoms[a]

Factors	LADG (n = 30)	Vs-LADG (n = 75)	p-value
Oral intake (%)	86 ± 14	82 ± 14	NS
Body weight (%)	92 ± 5	90 ± 6	NS
Symptoms: n (%)			
Heart burn	4 (13)	15 (20)	NS
Diarrhea	4 (13)	9 (12)	NS
Constipation	5 (17)	7 (9.3)	NS
Dumping syndrome	2 (6.7)	4 (5.3)	NS
Abdominal ultrasonography: n (%)			
Gallstone formation	4 (13)	1 (1.3)	<0.05
Blood chemistry			
Hemoglobin (g/dl)	12.7 ± 1.4	13.1 ± 2.0	NS
Albumin (mg/dl)	4.2 ± 0.3	4.2 ± 0.4	NS
Total-cholesterol (mg/dl)	182 ± 31	190 ± 30	NS

LADG, laparoscopically assisted distal gastrectomy; Vs-LADG, vagus nerve–sparing laparoscopically assisted distal gastrectomy; NS, not significant

[a] Data are given as the mean ± standard deviation or number

Discussion

Injury to the vagal nerve during gastrectomy is known to cause postvagotomy diarrhea and gallstone formation. Kennedy et al. [18] reported a higher incidence of postoperative diarrhea in gastrectomy with truncal vagotomy than in selective vagotomy for patients with duodenal ulcer. It is considered that gallstone after gastrectomy is caused by injury to hepatic branches from the anterior vagal trunk and autonomic nerves around the common hepatic artery. Injury to these nerves also reduces insulin secretion [19–21].

To prevent these disorders, preservation of the autonomic nerves has been introduced in conventional open gastrectomy for early gastric cancer [15, 22]. Recently, this autonomic nerve preservation has been combined with laparoscopic gastrectomy because laparoscopic surgery has the advantage of a magnified view that allows clear identification of the nerve branches [16, 23–25].

The current study showed that the incidence of gallstone 1 year after surgery is significantly lower with Vs-LADG than with LADG, and that Vs-LADG and LADG do not differ in operation time or bleeding. Uyama et al. [24] reported lower incidences of gallstone and diarrhea as a result of sparing vagal nerves. Tsuji et al. [26] reported in the Japanese literature that the frequency of gallstone formation indicative of vagus-preserving distal gastrectomy was 1.7%, whereas that for D2 distal gastrectomy without nerve preservation was 13.6% in open surgery, showing a statistically significant difference. On the other hand, Sakuramoto et al. [25] concluded that no functional benefit was observed with Vs-LADG, and that longer operating time and greater bleeding were disadvantages.

Although Uyama et al. [24] reported a lower incidence of diarrhea in gastrectomy with nerve preservation, we did not observe a reduced incidence of diarrhea or earlier recovery of BW. Bowel condition and BW may recover earlier than expected and stabilize within 1 year after surgery. Another possibility is that macroscopic morphologic preservation of the celiac branches does not mean functional preservation because there would have been dissection-induced microinjury of fine nerve fibers around the nerves. Interestingly, the time to first flatus tended to be shorter after Vs-LADG, which may be a favorable effect of sparing the celiac branches.

We have followed up only 1 year to evaluate gallstone formation. The effectiveness of vagus nerve preservation in decreasing the development of gallstones may be better evaluated by long-term follow-up studies.

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