Laparoscopic Versus Open Subtotal Gastrectomy for Distal Gastric Cancer

Five-Year Results of a Randomized Prospective Trial

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Objective: The aim of this study was to compare technical feasibility and both early and 5-year clinical outcomes of laparoscopic-assisted and open radical subtotal gastrectomy for distal gastric cancer.

Summary Background Data: The role of laparoscopic surgery in the treatment of gastric cancer has not yet been defined, and many doubts remain about the ability to satisfy all the oncologic criteria met during conventional, open surgery.

Methods: This study was designed as a prospective, randomized clinical trial with a total of 59 patients. Twenty-nine (49.1%) patients were randomized to undergo open subtotal gastrectomy (OG), while 30 (50.9%) patients were randomized to the laparoscopic group (LG). Demographics, ASA status, pTNM stage, histologic type of the tumor, number of resected lymph nodes, postoperative complications, and 5-year overall and disease-free survival rates were studied to assess outcome differences between the groups.

Results: The demographics, preoperative data, and characteristics of the tumor were similar. The mean number of resected lymph nodes was 33.4 ± 17.4 in the OG group and 30.0 ± 14.9 in the LG (P = not significant). Operative mortality rates were 6.7% (2 patients) in the OG and 3.3% (1 patient) in the LG (P = not significant); morbidity rates were 27.6% and 26.7%, respectively (P = not significant). Five-year overall and disease-free survival rates were 55.7% and 54.8% and 58.9% and 57.3% in the OG and the LG, respectively (P = not significant).

Conclusions: Laparoscopic radical subtotal gastrectomy for distal gastric cancer is a feasible and safe oncologic procedure with short- and long-term results similar to those obtained with an open approach. Additional benefits for the LG were reduced blood loss, shorter time to resumption of oral intake, and earlier discharge from hospital.

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The recommended treatment of distal gastric cancer consists of a radical resection of the distal 4/5 of the stomach with a free margin of 5 to 6 cm.[1–3] The extent of the associated lymph node dissection is still debated. Japanese authors suggest an extended dissection with the routine involvement of D1 and D2 lymph nodes, while an even wider (D3 and D4) dissection is advocated in cases of suspected invasion of more distant lymph nodes.[4–8] Western authors often prefer a limited dissection (D1) because of the higher operative mortality and morbidity rates associated with extended lymphadenectomy (D2),[9–13] even when distal pancreatectomy is avoided, as well as the lack of a significantly improved long-term survival data.[14–18]

In the past decade, laparoscopic techniques have gained wide clinical acceptance in surgical practice. This approach offers important advantages when compared with open surgery: reduced intraoperative blood loss, reduced postoperative pain and accelerated recovery, earlier return to normal bowel function with earlier resumption of oral intake, early discharge from hospital, and lower financial costs.[19–22]

The same advantages have been reported after laparoscopic subtotal or total gastrectomy for benign tumors as well as early gastric cancers.[23–31] However, laparoscopically assisted subtotal gastrectomy for distal gastric cancer can only be justified and widely accepted as a safer alternative to open surgery if equal long-term results are obtained. This would suggest an equivalent radical oncologic resection.

The purpose of our study was to compare early and 5-year results of subtotal gastrectomy performed for distal gastric cancer using both a laparoscopic and an open approach, therefore defining the role of laparoscopic surgery in the treatment of this disease.

MATERIALS AND METHODS

Between November 1992 and February 1996, 70 patients with a preoperative diagnosis of distal gastric cancer were considered for subtotal gastrectomy at our institution. Patients were prospectively randomized to undergo an open

(OG, open group, 35 patients, 50%) or a laparoscopic (LG, laparoscopic group, 35 patients, 50%) surgical approach, having given informed consent. Randomization was performed in a single-blind fashion by the team who admitted the patients. A single experienced laparoscopic surgeon (C.G.S.H.) was made aware of the randomization at the operating table, and he performed all the procedures.

For the purpose of this study, we excluded 11 (15.7%) patients who at the initial open (n = 6) or laparoscopic (n =5) exploration presented with metastatic tumor (2 patients, 2.8%) or extension of the tumor beyond the distal stomach (9 patients, 12.9%). Thus, the study group consisted of 59 patients (39 males and 20 females; mean age, 63.6 ± 12.7 years; range, 38–81 years) submitted to either open (OG, 29 patients, 49.1%) or laparoscopic (LG, 30 patients, 50.9%) radical subtotal gastrectomy.

Demographics, surgical risk (ASA status determined according to the standard proposed by the American Society of Anesthesiology[32]), pTNM stage, histologic pattern of the tumor (according to the Lauren classification[33]), duration of surgery, type of gastrointestinal reconstruction, number of resected lymph nodes, estimated blood loss, preoperative and postoperative hemoglobin, postoperative complications and length of stay, time to resuming food intake, and 5-year overall and disease-free survival rates were studied to assess outcome differences between the 2 groups. Patient status was determined by follow-up examination.

Operative Technique of Laparoscopic Distal Subtotal Gastrectomy

The procedure is carried out under general anesthesia with endotracheal intubation and epidural analgesia. The patient lies on the table in the supine position, with legs apart and 20° head-up tilt. The surgeon operates in the "French" position with the camera assistant on his left.

CO_2 pneumoperitoneum is induced after insertion of the first 10/12-mm cannula at the level of the umbilicus, with a modified open technique. The stomach and the peritoneal cavity are inspected to rule out adjacent organ invasion and peritoneal seeding. Three other trocars are inserted through the abdominal wall, one in the left upper quadrant, one in the right upper quadrant and one in the midline, just below the xyphoid process. At this stage, intraoperative laparoscopic ultrasonography is carried out to scan the liver surface and assess the presence of deep liver metastases.

The gastrocolic ligament is divided using the ultrasonically activated scissors (Ultracision–Harmonic Scalpel, Ethicon Endo-Surgery Inc, Cincinnati, OH) along the border of the transverse colon, thus including the greater omentum in the specimen to be resected. The dissection is continued to the right toward the pylorus to include the group of infra-pyloric lymph nodes (group 6). The right gastroepiploic vessels are divided either between clips flush with anterior surface of the pancreas, coagulated and divided by the harmonic scissors or stapled-divided after careful preparation to avoid inadvertent compromise of lymph nodes. The lymph nodes along the pancreatoduodenal artery (group 17) may also be removed at this stage. The Kocher maneuver is accomplished, allowing dissection of the retropancreatic nodes (group 13). The first part of the duodenum is dissected and transected with a 35- or 45-mm cartridge endostapler. The lymph nodes of the hepatoduodenal ligament are dissected and removed en bloc. To accomplish the dissection, a cholecystectomy is performed and the elements of the hepatic pedicle (bile duct, left hepatic artery, right hepatic artery, and portal vein) are carefully isolated and encircled with umbilical tapes. Gentle traction on these structures facilitates and expedites the dissection of nodes. The right gastric artery is divided with the ultrasonically activated scissors at its origin from the common hepatic artery. The lymph node dissection is continued to the left along the common hepatic artery (group 8), celiac axis (group 9), left gastric artery (group 7), and proximal splenic artery (group 11b). Residual oozing after lymph node dissection both along the anterior aspect of the pancreas and the lesser omentum is best controlled by argon plasma coagulation. The left gastric vessels are best approached from below after gentle cephalad traction on the stomach with the greater omentum folded up on the anterior aspect of the stomach. The vessels are carefully prepared and separately divided, the vein using harmonic scissors and the artery with an endostapler. The dissection of the gastrocolic ligament is continued toward the spleen; the left gastroepiploic artery is divided either with the harmonic scissors or the endostapler; only the first 2 short gastric vessels are divided using harmonic scissors. Before stomach transection, the cardiac nodes are dissected en bloc: the right cardiac nodes (group 1) are approached continuing the line of dissection of lymph nodes along the left gastric artery. Left cardiac nodes (group 2) are not necessarily dissected for cancer of the distal third of the stomach. When dissected, cephalad traction on the stomach and anterior truncal vagotomy ease the removal of lymphatic tissue. The transection of the stomach and resection of the distal 4/5 of the organ are accomplished by multiple endostapler applications (either 35-mm or 45-mm cartridges).

A 50-cm transmesocolic Roux-en-Y loop is prepared and anastomosed side-to-side to the posterior wall of the gastric stump with a single or double application of endostapler (45- vs. 35-mm cartridge). Interrupted hand sutures (90-cm long 2-0 monofilament polypropylene) with extracorporeal slipknots then close the access opening on the jejunal limb and the gastric stump. A side-to-side jejunojejunal anastomosis at the foot of the Roux-en-Y loop is fashioned by further endostapler application and, finally, the access opening on the jejunal limbs is hand sutured.

The Billroth II reconstruction is performed similarly: a transmesocolic, isoperistaltic side-to-side gastrojejunal anastomosis on the posterior gastric wall is fashioned by single or

double endostapler application, at a distance of 30 cm from the ligament of Trietz. The access opening on the gastric stump and the jejunum is then closed with interrupted 2-0 or 3-0 polypropylene hand sutures tied by extracorporeal slip-knots. The specimen, inserted into a retrieval bag, is withdrawn through the large-bore cannula.

Statistical Analysis

The data were entered into a computer spreadsheet (Microsoft Excel XP for Windows; Microsoft, Redmond, WA). Statistical comparisons were obtained with the software package SPSS (Basic and advanced program, version 10.0.7; SPSS Inc. Chicago, IL). All values are expressed as the mean ± the standard error of the mean. The comparisons among groups were tested with ANOVA and Pearson χ^2 test, with Yates correction for conditional variables. Overall and disease-free survival rates were assessed by Kaplan-Meier analysis. Comparisons between curves were performed by the Wilcoxon rank sum test. Significance was taken at the level of the P value less than 0.05.

RESULTS

Open Group

Twenty-nine (49.1%) patients (21 males and 8 females; mean age 63.6 ± 13.2 years; range, 40–81 years) were operated on using the open approach. Surgical risks were classified as ASA 1 in 7 (24.1%) patients, ASA 2 in 14 (48.3%), and ASA 3 in 8 (27.6%) patients.

The operation performed was a D1 resection in 9 (31.0%) patients and a D2 resection in 20 (69.0%) patients, with a mean number of lymph nodes dissected of 33.4 ± 17.4 (range, 4–67 lymph nodes). A Roux-en-Y reconstruction was performed in 22 (75.9%) cases and a Billroth II reconstruction in 7 (24.1%) patients. The length of resection was 10.7 ± 1.8 cm on the lesser curve and 16.9 ± 2.7 cm on the greater curve. The clear margin of the resected tumor was 6.3 ± 0.7 cm (range, 5–7 cm). The operative time was 168 ± 29 minutes. The estimated blood loss was 391 ± 136 mL.

Preoperative and postoperative Hb values were 11.9 ± 1.8 g/dL (range, 8–15 g/dL) and 10.0 ± 1.9 g/dL (range, 6–14 g/dL), respectively. The pTNM is reported in Table 1. Stages of the tumor were IA in 6 (20.7%) patients, IB in 6 (20.7%), II in 4 (13.8%), IIIA in 5 (17.2%), IIIB in 3 (10.4%) and IV in 5 (17.2%) patients. Histologic type of the tumor was intestinal in 18 (62.1%) patients and diffuse in 11 (37.9%). Thirty-day mortality and morbidity results included 2 postoperative deaths caused by adult respiratory distress syndrome and myocardial infarction, 1 postoperative major complication, and 7 minor complications (Table 2). These features represent a 6.7% mortality rate and a 27.6% morbidity rate. Patients resumed oral food intake by 7.4 ± 2.0 days and were discharged after 14.5 ± 4.6 days (range, 9–31 days). Long-term follow-up was available for all patients for an average of 49.7 ± 5.2 months (range, 7–90 months; median, 55 months). The rate of disease recurrence was 37.0% (10 patients). All of the patients died of their primary disease. Five-year overall and disease-free survival rates were 55.7% (with 8 patients still alive after 60 months) and 54.8%, respectively.

TABLE 1. TNM of Patients According to the 1997 AICC pTNM Staging System[38]

	OG (29 patients) [no. (%)]	LG (30 patients) [no. (%)]
T1 N0 (S IA)	6 (20.8)	7 (23.3)
T2 N0 (S IB)	3 (10.3)	6 (20.0)
T2 N1 (S II)	3 (10.3)	3 (10.0)
T3 N0 (S II)	2 (6.7)	1 (3.3)
T3 N1 (S IIIA)	6 (20.8)	5 (16.7)
T4 N0 (S IIIA)	1 (3.5)	—
T3 N2 (S IIIB)	4 (13.8)	3 (10.0)
T4 N1 (S IV)	3 (10.3)	5 (16.7)
T4 N2 (S IV)	1 (3.5)	—

TABLE 2. Causes of Postoperative Morbidity

	OG [no. (%)]	LG [no. (%)]
Total	8 (27.6)	7 (23.3)
Duodenal stump leak	1 (12.5)	—
Edematous pancreatitis	—	1 (14.3)
Pleural effusion	3 (37.5)	3 (42.8)
Bronchopneumonia	2 (25.0)	1 (14.3)
Wound infection	2 (25.0)	2 (28.6)

Laparoscopic Group

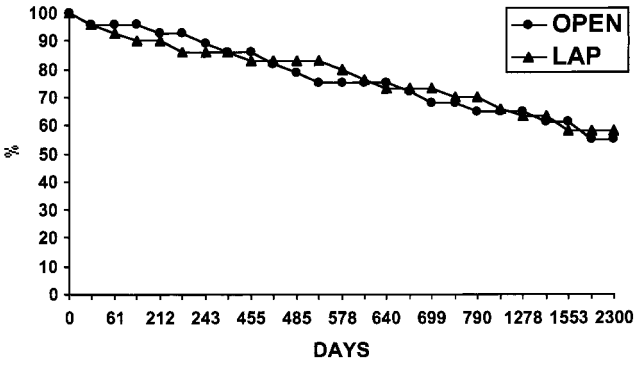
Thirty (50.9%) patients (18 males and 12 females; mean age, 63.2 ± 12.5 years; range, 38–81 years) were operated on with the laparoscopic approach. Surgical risks were classified as ASA 1 in 10 (33.3%) patients, ASA 2 in 10 (33.3%), and ASA 3 in 10 (33.3%) patients.

The operation performed was a D1 resection in 9 (30.0%) patients and a D2 resection in 21 (70.0%) patients, with a mean number of lymph nodes dissected of 30.0 ± 14.9 (range, 7–66 lymph nodes). A Roux-en-Y reconstruction was performed in 25 (83.3%) cases and a Billroth II reconstruction in 5 (16.7%) patients. The length of resection was 10.9 ± 1.9 cm on the lesser curve and 18.0 ± 2.7 cm on the greater curve. The clear margin of the resected tumor was 6.9 ± 0.8 cm (range, 6–8 cm). The operative time was 196 ± 21 minutes. The estimated blood loss was 229 ± 144 mL.

Preoperative and postoperative Hb values were 12.9 ± 1.1 g/dL (range, 11–16 g/dL) and 12.0 ± 4.7 g/dL (range, 8–15 g/dL), respectively. The pTNM is reported in Table 1. Stages of the tumor were IA in 7 (23.3%) patients, IB in 3 (10.0%), II in 5 (16.7%), IIIA in 7 (23.4%), IIIB in 4 (13.3%), and IV in 4 (13.3%) patients. Histologic type of the tumor was intestinal in 16 (53.3%) cases and diffuse in 14 (46.7%). Thirty-day mortality and morbidity results included one postoperative death caused by adult respiratory distress syndrome and 8 minor complications (Table 2). These features represent a 3.3% mortality rate and a 26.7% morbidity rate. Patients resumed oral food intake by 5.1 ± 0.5 days and were discharged by 10.3 ± 3.6 days (range, 6–21 days). Long-term follow-up was available for all patients for an average of 52.2 ± 26.5 months (range, 2–88 months; median, 60 months). The rate of disease recurrence was 37.9% (11 patients). All of the patients with recurrences died of their primary disease. No port-site metastases were observed. Five-year overall and disease-free survival rates were 58.9% (with 9 patients still alive after 60 months) and 57.3%, respectively.

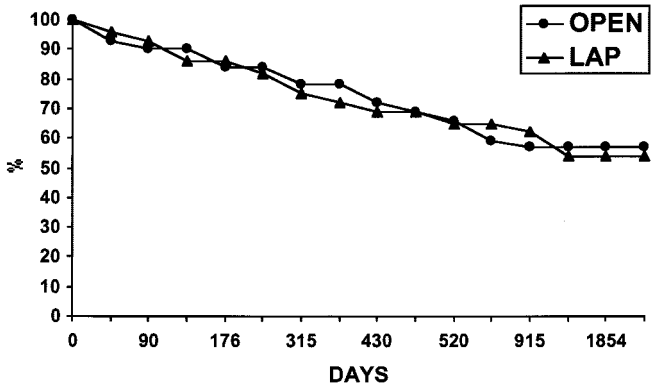
Comparative Results

No statistical differences were observed between the 2 groups in terms of demographics, ASA status, pTNM stage, histologic type of the tumor, duration of surgery, type of gastrointestinal reconstruction, number of resected lymph nodes, and preoperative and postoperative hemoglobin. In the OG, a higher estimated blood loss ($P < 0.001$) was recorded when compared with the LG. Postoperative mortality and morbidity rates were similar between the groups (P = not significant). Earlier resumption of food intake and discharge home were observed in the LG ($P < 0.001$ and $P < 0.001$, respectively). Figures 1 and 2 show similar survival rates and disease-free intervals (P = not significant). No statistical differences in the incidence of unrelated deaths and 5-year recurrence rates were observed between the 2 groups (P = not significant).



DAYS	0	30	61	181	213	243	458	485	488	578	641	699	731	790	823	1278	1341	1553	1854	2300
OPEN	29	28	28	28	27	25	24	23	22	22	21	20	20	19	19	18	17	12	8	1
LAP	30	29	28	27	26	26	25	25	25	23	22	22	21	21	20	18	18	11	9	2

FIGURE 1. Overall survival rates of LG and OG patients. Numbers at the bottom are the patients alive at the beginning of each interval.



DAYS	0	30	90	131	176	198	315	344	430	502	520	631	915	1439	1854	2300
OPEN	29	28	27	25	25	24	22	21	20	20	19	19	18	14	8	1
LAP	30	28	27	27	26	26	25	25	23	22	21	20	19	17	9	2

FIGURE 2. Disease-free survival rates of LG and OG patients. Numbers at the bottom are the patients alive at the beginning of each interval.

DISCUSSION

Gastric cancer remains among the top 10 causes of cancer-related deaths for both men and women.[2] Radical surgical resection of the tumor is the only hope for cure in these patients.[2,12] Total gastrectomy has been advocated for proximal and middle stomach cancer. However, for distal gastric cancer, results have been similar for total and subtotal gastrectomy and the latter is now the operation of choice when the tumor is located in the distal part of the stomach.[1–3] Discussion remains open about the extent of lymphadenectomy. Several authors, especially the Japanese, advocate a D2 or D3 lymphadenectomy, because of improved long-term survival, despite the higher postoperative morbidity and mortality.[4–8]

Our policy in the treatment of distal gastric cancer includes open or laparoscopic subtotal gastrectomy with D2 lymphadenectomy. However, in high-risk patients with an early stage gastric cancer, we perform a D1 lymphatic dissection to reduce postoperative complications. In these patients, we also perform a Billroth II retrocolic gastrojejunostomy instead of a Roux-en-Y reconstruction to shorten the operative time.

Officially, the first laparoscopic-assisted distal gastrectomy with a Billroth II gastrojejunostomy was performed by Goh et al in 1992, for the treatment of a complicated peptic ulcer.[34] The first laparoscopic gastrectomy, with a Billroth II reconstruction, for cancer was performed by Kitano et al in 1992 and published in 1994.[35] Subsequently, several authors

have reported successful laparoscopic subtotal or total gastrectomy, demonstrating the important postoperative advantages of this procedure.[23–31]

In 1997, Goh et al published the early results of 118 laparoscopic-assisted distal gastrectomy performed for benign and neoplastic disease by 16 surgeons in 12 countries who responded to a questionnaire: 10 surgeons claimed laparoscopic distal gastrectomy to be superior to open distal gastrectomy due to faster recovery, reduced pain, and better cosmesis.[36] Adachi et al[25] reported the results of a questionnaire on the quality of life after a laparoscopic assisted Billroth gastrectomy. The responses of the 76 patients showed that laparoscopic distal gastrectomy was significantly better than open distal gastrectomy with respect to weight loss, difficulty in swallowing, heartburn, or belching and early dumping syndrome.[25] The same authors in 2000 reported the results of a comparative clinical study between laparoscopic and open distal gastrectomies demonstrating the superiority of the former in terms of surgical trauma, rapid return of gastrointestinal function, and shorter hospital stay.[26] Finally, in 2002 Kitano et al published a randomized clinical trial on 28 patients affected with an early gastric cancer and submitted to laparoscopic assisted or open distal gastrectomy with Billroth reconstruction.[27] The authors evaluated surgical impairment of pulmonary functions (forced vital capacity and forced expiratory volume in 1 second) measured preoperatively and on third postoperative day, and postoperative pain during resting, coughing, and walking by a visual analog scale. The results of this study showed an earlier recovery, less pain, and reduced impairment of pulmonary function after laparoscopic assisted distal gastrectomy.

Despite these encouraging results, at present, many doubts still remain about the ability, during the video-assisted laparoscopic procedure, to satisfy all the oncologic criteria met during conventional, open surgery in gastric cancer patients. In 1999, Shirasihi et al reported a series of 40 laparoscopic assisted Billroth gastrectomies and lymphadenectomies for early cancer of the antrum and gastric body, with no postoperative morbidity and mortality and no recurrence at a mean follow-up of 21 months.[24] In addition, Kitano et al did not observe differences in terms of curability, at a mean follow-up of 21.5 months, in their prospective and randomized series.[27] In 2003, Weber et al published the results of their comparative study between a series of 12 patients affected with a gastric cancer and treated by a laparoscopic gastrectomy, and a series of 13 matched open controls. They did not observe differences between the groups in terms of stage of disease, radical resection, extent of lymphadenectomy, and 18-month survival rates.[37] As far as we know, this is the first prospective and randomized trial comparing 5-year results of subtotal gastrectomy performed for distal gastric cancer with laparoscopic and open approaches. Patients' characteristics were similar, as demonstrated by the lack of differences in demographics, ASA status, pTNM stage, size, and grading of the tumor.

A radical resection was performed in both groups of patients. All specimens were measured at the end of operation, showing a similar length of resection at the level of both lesser and greater gastric curvatures. Free margins of resection were at 5 to 6 cm from the tumor in all patients, as indicated to ensure a low rate of anastomotic recurrence. The mean number of resected lymph nodes was similar in both groups. Thus, the laparoscopic approach did not limit the feasibility of an oncologically correct resection of the gastric tumor and extended lymphadenectomy. Moreover, 5-year overall and free-disease survival rates were not influenced by the surgical approach, confirming the radicality of the laparoscopic resection. As in other laparoscopic procedures, we observed important operative and postoperative advantages in LG patients: lower intraoperative blood loss, earlier resumption of oral intake, and earlier discharge from hospital. These results offer a clear answer to our initial question: in experienced hands, laparoscopic-assisted subtotal gastrectomy for distal gastric cancer is a feasible and safe alternative to open, standard gastric resection, with similar short- and long-term results that testify to the oncologic radicality of the procedure. However, laparoscopic gastric surgery is demanding from a technical point of view, especially when a D2 lymphadenectomy is performed. Adequate training in laparoscopic techniques and procedures is mandatory prior to embarking on a laparoscopic gastrectomy.

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