

Short-term efficacy of laparoscopy-assisted vs open radical gastrectomy in gastric cancer

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(103.1 ± 19.5 mL vs 163.0 ± 32.9 mL, $P < 0.0001$), shorter postoperative hospital stay (6.8 ± 1.2 d vs 9.5 ± 1.6 d, $P < 0.0001$), less frequent occurrence of postoperative complications (6.5% vs 13.5%, $P = 0.02$), shorter time to mobilization (1.0 ± 0.3 vs 3.3 ± 0.4 d, $P < 0.0001$), shorter time to bowel opening (3.3 ± 0.7 d vs 4.5 ± 0.7 d, $P < 0.0001$), and shorter time to normal diet (3.0 ± 0.4 vs 3.8 ± 0.5 d, $P < 0.0001$). However, LARG required a longer time to complete than the ORG procedure (192.3 ± 20.9 min vs 180.0 ± 26.9 min, $P < 0.0001$).

CONCLUSION: Compared to ORG, LARG is safer, more effective, and less invasive for treating gastric cancer, with better short-term efficacy.

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Key words: Laparoscopic surgery; Gastric cancer; Short-term efficacy; Open surgery

Abstract

AIM: To investigate the short-term benefits of laparoscopic radical gastrectomy (LARG) and open radical gastrectomy (ORG) in patients with gastric cancer.

METHODS: A total of 400 patients with gastric cancer aged ≤ 65 years who were treated at General Hospital of Lanzhou Military Region were enrolled. Among these, 200 patients underwent LARG between October 2008 and August 2012 (LARG group); and 200 patients underwent ORG between March 2000 and September 2008 (ORG group). The short-term therapeutic benefits between the two groups were analyzed.

RESULTS: The LARG procedure offered significantly better benefits to the patients compared to the ORG procedure, including less intraoperative blood loss

Core tip: We compared patients who underwent laparoscopic-assisted radical gastrectomy (LARG) with those who underwent open radical surgery (ORG) in terms of intra- and postoperative benefits. LARG was successfully completed without needing to convert to laparotomy in all patients, and no residual cancerous tissues were noted in the surgical margins. LARG offered the patients several better short-term benefits compared to the ORG procedure, such as less intraoperative blood loss, shorter hospitalization time, shorter time to mobilization, and shorter time to bowel opening. Additionally, LARG was also associated with fewer postoperative complications.

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INTRODUCTION

Gastric cancer is one of the most common malignant tumors worldwide, with a yearly incidence of about 900000. In China, > 400000 cases of gastric cancer are diagnosed annually, and the mortality rate is estimated to be 25.2/100000, which accounts for 23.3% of cancer-related mortality^[1]. The 5-year survival rate is about 95% for early gastric cancer but, in patients with advanced gastric carcinoma, the 5-year survival falls to < 50%^[2]. In China, > 90% of gastric cancer patients are diagnosed at an advanced stage when they first present^[1].

At the present time, radical surgery is the only effective treatment for early gastric cancer with a potential to cure the disease^[3]. Since its seminal application in patients with advanced gastric cancer in 1991 by a group of Japanese surgeons^[4], laparoscopic radical gastrectomy (LARG) has been increasingly used as a promising approach for the management of gastric cancer because of its minimal invasiveness and its potential to treat successfully patients with lymph node metastasis^[5,6]. However, LARG is technically demanding and requires a long learning curve^[4,7].

Although LARG and laparoscopic D2 gastrectomy have now been widely used in the treatment of gastric cancer, including advanced gastric carcinoma, the short- and long-term benefits are unclear. The short-term outcomes of LARG have recently been reported, although these studies were based on small samples.

In the current study, we compared the short-term outcomes between LARG and open radical gastrectomy (ORG) in patients with gastric cancer in our department.

MATERIALS AND METHODS

Patient selection criteria

A total of 200 patients with gastric cancer who were treated with LARG after 2008 were randomly selected (LARG group). Tumors were located in the antrum ($n = 95$), cardia-fundus ($n = 56$), and corpus ($n = 49$) of the stomach. Pathological diagnosis of gastric cancer was confirmed in all patients using gastroscopic biopsy specimens. These samples included adenocarcinoma ($n = 156$), signet ring cell carcinoma ($n = 15$), adenosquamous carcinoma ($n = 6$), squamous cell carcinoma ($n = 8$), carcinoid ($n = 4$), and undifferentiated carcinoma ($n = 11$). The pathological classification was based on the 2010 World Health Organization (WHO) classification^[8].

We also randomly selected 200 patients with gastric cancer who were treated with ORG between 2000 and 2008 (ORG group). Within this group, tumors were located in the antrum ($n = 91$), cardia-fundus ($n = 58$), and corpus ($n = 51$) of the stomach. Pathological diagnosis was confirmed in all patients using gastroscopic biopsy

specimens, including adenocarcinoma ($n = 162$), signet ring cell carcinoma ($n = 10$), adenosquamous carcinoma ($n = 7$), squamous cell carcinoma ($n = 6$), carcinoid ($n = 7$), and undifferentiated carcinoma ($n = 8$), based on the 2010 WHO classification^[8].

Surgical procedures

Patients fasted for 24 h prior to surgery. Following general anesthesia and endotracheal intubation, patients were placed in the supine position with their legs apart. A small subumbilical arc incision of 1 cm was made, and a pneumascos needle was inserted to generate CO₂ pneumoperitoneum, which was maintained at 12-14 mmHg during surgery. A 10-mm trocar was inserted into the same incision, and laparoscopy-assisted examination was performed to assess visually the extension, diameter, and location of the lesion. Tumor metastasis, serous layer invasion, adhesion to adjacent tissues, and organs were also carefully examined to determine the best angle of approach. A 12-mm trocar was inserted at the junction of the left lower costal margin and anterior axillary line to conduct the operation. Three 5-mm trocars were inserted through the abdominal wall; one at the level of the umbilicus at the left midclavicular line; one at the junction of the right lower costal margin and right midclavicular line; and one at the junction of the right lower costal margin and anterior axillary line. The operator was standing on the left side of the patient, while one assistant was standing on the right side, and another assistant who was holding the laparoscope was standing between the patient's legs. Blocking glue was used at the serous layer of the tumor to prevent implantation metastasis, and biological glue was used to seal the anastomosis after the tumor was removed completely to prevent the formation of anastomotic leakage or stump fistula.

Radical distal subtotal gastrectomy

The greater omentum was resected off the transverse colon using an ultrasonic knife along the border of the transverse colon. The dissection was continued to the left toward the splenic flexure, and to the right toward the origin of right gastroepiploic artery. The anterior lobe of the transverse mesocolon and pancreatic capsule were also resected, and lymph nodes along the middle colic artery were removed. The right gastroepiploic artery and the right gastro-omental vein were isolated and resected after ligation using titanium clips, and lymph nodes (Group 6) were removed. The greater omentum was pulled to the front of the stomach, and the stomach was gently picked up. The common hepatic artery, splenic artery, and left gastric artery were dissected, and the lymph nodes of Groups 8, 11, 7 and 9 were removed. The left gastric artery was ligated by two titanium clips and resected. The hepatogastric ligament and right gastric artery were resected along the lesser curvature, and the lymph nodes of Groups 5, 12, 3, 1 and 4 were removed. A longitudinal incision of 5 cm was made in the center of the upper abdomen. After an incision protective layer

Table 1 Patients characteristics *n* (%)

	LARG	ORG	<i>P</i> value
Sex (male/female)	109/91	112/88	0.84
Age (yr)	58.3 ± 6.5	58.6 ± 6.3	
Pathological type			
Well-differentiated adenocarcinoma	49 (24.5)	38 (19.0)	0.32 ¹
Moderately-differentiated adenocarcinoma	23 (11.5)	31 (15.5)	
Poorly-differentiated adenocarcinoma	115 (57.5)	122 (61.0)	
Signet ring cell carcinoma	13 (6.5)	9 (4.5)	
Classification (T)			
T1	18 (9.0)	15 (7.5)	0.86 ²
T2	89 (44.5)	91 (45.5)	
T3	93 (46.5)	94 (47.0)	
Lymph node metastasis			
N0	13 (6.5)	11 (5.5)	0.90 ³
N1	88 (44.0)	91 (45.5)	
N2	99 (49.5)	98 (49.0)	
Clinical stage			
I + II	91 (45.5)	89 (44.5)	0.92
III + IV	109 (54.5%)	111 (55.5)	

¹Well-differentiated adenocarcinoma group of LARG and ORG; ²T1 group of LARG and ORG; ³I + II group of LARG and ORG. LARG: Laparoscopic radical gastrectomy; ORG: Open radical gastrectomy.

was placed, the stomach was pulled out of the abdominal cavity, and the distal part of the stomach was resected. A Billroth I or II reconstruction was then performed. The abdominal cavity was perfused with low-permeability, warm sterilized distilled water for 30 min. The distilled water was discarded, and the peritoneal cavity was perfused with 1 g Tegafur and 0.3 g leucovorin in 250 mL saline. The abdomen was closed after drainage tubes were placed.

Radical proximal subtotal gastrectomy

The greater omentum, anterior lobe of the transverse mesocolon, and pancreatic capsule were isolated along the border of the transverse colon to the splenic flexure, and the right gastroepiploic hemal arch was kept intact at the distal greater curvature. The lymph nodes of Groups 6 and 4 were removed. The splenic flexure was isolated, and the left gastroepiploic artery and vein were dissected. The short gastric vessel was resected at the origin. The splenic artery was isolated and the lymph nodes of Groups 11 and 10 were removed. The stomach was isolated from the gastric fundus and posterior stomach, and the lymph nodes of Groups 8, 9 and 7 were removed. The lesser omentum was isolated along the inferior border of the liver, 5 cm of the esophagus was exposed, and the cardia was dissected. The anterior and posterior vagal trunks were resected, and the lymph nodes of Groups 1-3 were removed. A longitudinal incision of 5 cm was made in the center of the subcostal area. The same procedures to protect the incision were performed as for radical distal subtotal gastrectomy as described above, and the stomach was pulled out of the abdominal cavity. After the proximal part of the stomach was resected, the

anterior wall of the residual stomach was resected, and staples were placed. The esophagus and residual stomach were anastomosed, and the anterior wall of the stomach was stitched. The abdominal cavity was perfused with low-permeability, warm sterilized distilled water for 30 min. The distilled water was discarded, and peritoneal perfusion with chemotherapy drugs was performed. The abdomen was closed after drainage tubes were placed.

Radical total gastrectomy

The veins and lymph nodes were isolated and removed in the same way as in subtotal gastrectomy. A longitudinal incision of 5-7 cm was made in the center of the upper abdomen. The same procedures were performed to protect the incision as in radical distal subtotal gastrectomy, and the stomach was pulled out of the abdominal cavity. The cardia was then resected, and the whole stomach and lymph nodes around the omentum were removed. Roux-en-Y reconstruction was performed. The abdominal cavity was perfused with low-permeability, warm sterilized distilled water for 30 min. The distilled water was discarded, and peritoneal cavity was perfused as described above. The abdomen was closed after drainage tubes were placed.

ORG

The operation was carried out under general anesthesia with endotracheal intubation. Patients were placed in the supine position. An incision of 15-20 cm was made in the center of the upper abdomen. Radical gastrectomy was performed as described above.

Outcomes

The readout outcomes selected to assess the therapeutic efficacy were: operation time, number of lymph nodes dissected, intraoperative blood loss, length of hospital stay, time to mobilization, time to bowel opening, and time to normal diet.

Statistical analysis

Statistical analysis was performed using SPSS 18.0 (SPSS Inc., Chicago, IL, United States). Continuous data are presented as mean ± SD, and were analyzed using Student's *t* test. Categorical data are presented as proportions, and were analyzed using the χ^2 test. *P* < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

A total of 200 patients, including 109 men and 91 women with a mean age of 56.1 years (range: 23-63 years) were included in the LARG group. In the ORG group, there were 112 men and 88 women with a mean age of 56.3 years (range: 21-65 years). No significant differences were observed between the two groups in terms of age, sex, pathological type of tumor, depth of tissue invasion, lymph node metastasis, and clinical stage (Table 1).

Table 2 Comparison of surgical outcomes between laparoscopic radical gastrectomy and open radical gastrectomy groups

Outcomes	LARG	ORG	P value
Operation time (min)	192.3 ± 20.9	180.0 ± 26.9	< 0.0001
No. of lymph nodes removed	28.5 ± 4.5	28.3 ± 3.4	0.62
Intraoperative blood loss (mL)	103.1 ± 19.5	163.0 ± 32.9	< 0.0001
Bedbound time (d)	1.0 ± 0.3	3.3 ± 0.4	< 0.0001
Time to bowel opening (d)	3.3 ± 0.7	4.5 ± 0.7	< 0.0001
Length of incision (cm)	5.2 ± 0.7	17.8 ± 1.0	< 0.0001
Time to normal diet (d)	3.0 ± 0.4	3.8 ± 0.5	< 0.0001
Total hospital stay (d)	6.8 ± 1.2	9.5 ± 1.6	< 0.0001

LARG: Laparoscopic radical gastrectomy; ORG: Open radical gastrectomy.

Major intraoperative characteristics and outcomes

LARG was successfully performed in the 200 patients without conversion to laparotomy. ORG was also successfully performed in 200 patients. No malignant tissues were found at the lower or upper resection margin in any of the patients.

Table 2 shows the treatment characteristics between the two groups. Longer time was needed for LARG than for ORG (192.3 ± 20.9 min *vs* 180.0 ± 26.9 min, respectively, $P < 0.0001$). A similar number of lymph nodes was removed by both approaches ($P = 0.62$). The LARG procedure was superior to ORG for several outcomes, including: less intraoperative blood loss (103.1 ± 19.5 mL *vs* 163.0 ± 32.9 mL, $P < 0.0001$); less bedbound time (1.0 ± 0.3 d *vs* 3.3 ± 0.4 d, $P < 0.0001$); less time to bowel opening (3.3 ± 0.7 d *vs* 4.5 ± 0.7 d, $P < 0.0001$); less time to normal diet (3.0 ± 0.4 d *vs* 3.8 ± 0.5 d, $P < 0.0001$); and shorter hospital stay (6.8 ± 1.2 d *vs* 9.5 ± 1.6 d, $P < 0.0001$). In addition, the incision length was shorter in the LARG group than in the ORG group (5.2 ± 0.7 *vs* 17.8 ± 1.0 cm, $P < 0.0001$), and fewer patients required special pain control in the LARG group than in the ORG group (39.5% *vs* 56.5%, $P = 0.0007$).

Postoperative complications

As shown in Table 3, significantly fewer patients in the LARG group suffered from poor incision healing (2.5% *vs* 8.0%, $P = 0.01$) and pulmonary infection (2.0% *vs* 9.5%, $P = 0.001$). Fewer patients experienced anastomotic leakage or stump fistula in the LARG group than ORG group, although the difference was not significant (3.5% *vs* 7.5%, $P = 0.08$). No difference was observed in the incidence of decreased gastrointestinal motility and acute organ (liver or kidney) failure between the LARG and ORG groups ($P > 0.05$). Overall, the LARG group was associated with less frequent complications than the ORG group was (13% *vs* 27%, $P = 0.02$).

DISCUSSION

We compared 200 patients who underwent LARG and 200 who underwent ORG in terms of their intra- and postoperative benefits. The laparoscopic procedures were successfully completed without needing to convert to

Table 3 Comparison of postoperative complications between the two groups *n* (%)

Postoperative complications	LARG	ORG	P value
Decreased gastrointestinal motility	3 (1.5)	7 (3.5)	0.2
Anastomotic leakage/stump fistula	7 (3.5)	15 (7.5)	0.08
Poor incision healing	5 (2.5)	16 (8.0)	0.01
Pulmonary infection	4 (2.0)	19 (9.5)	0.001
Acute liver/kidney failure	1 (0.5)	4 (2.0)	0.18
Total	13 ¹ (6.5)	27 ¹ (13.5)	0.02

¹Some patients had two or more concomitant complications. LARG: Laparoscopic radical gastrectomy; ORG: Open radical gastrectomy.

laparotomy in all patients in the LARG group, and no residual cancerous tissues were noted in the surgical margins. Despite a significantly longer operation time with LARG, this approach offered the patients several better short-term benefits compared to the ORG procedure, such as less intraoperative blood loss, shorter hospitalization time, shorter time to mobilization, shorter time to bowel opening, and shorter time to normal dietary intake. Additionally, LARG was also associated with fewer postoperative complications.

Well-exposed surgical fields could help reduce blood vessel damage and reduce intraoperative blood loss. A satisfactory surgical field can be obtained using laparoscopy with the assistance of an ultrasonic knife and titanium clips, and this could greatly reduce intraoperative blood loss. Currently, the same surgical processes used in traditional radical gastrectomy are still used in LARG, including blood vessel ligation at the origin, excessive margin resection, and removal of perigastric lymphoid tissues. However, because LARG is performed with laparoscopic instruments inside the abdominal cavity, mechanic organ damage by direct contact with the stomach during surgery can be minimized.

The indications for LARG in the treatment of patients with gastric cancer vary among different centers. For example, Kitano *et al*^[9] have suggested that LARG could be indicated for patients with advanced-stage gastric carcinoma with an invasion depth lower than T2^[9,10], whereas Huscher *et al*^[11] have suggested that LARG is the best choice for patients with advanced gastric carcinoma in whom tumor invasion has reached T3^[11]. Based on our study, we believe that LARG is a safe, effective, and minimally invasive approach for treatment of gastric cancer, as previously reported^[7,12,13]. The long-term efficacy of LARG in patients with gastric cancer has also been reported^[10]. In this long-term follow-up study, no significant difference in the 5-year survival rate was observed between 136 patients with gastric cancer who underwent LARG and 120 who underwent ORG.

Currently, CO₂ pneumoperitoneum is widely used in LARG procedures. However, the use of CO₂ pneumoperitoneum could result in inhibition of the immune response in the abdominal cavity. In an animal experiment^[14], a significant decrease in the number of CD4/CD8 cells was observed after the induction of CO₂ pneu-

moperitoneum. CO₂ pneumoperitoneum was also shown to inhibit macrophage activation in the abdominal cavity, and thus inhibit the release of tumor necrosis factor (TNF)- α and interleukin-1 by macrophages. Both macrophages and TNF- α play a potent role in the antitumor activity in the abdominal cavity^[15].

During the treatment of malignant tumors using laparoscopy-assisted approaches, potential tumor implantation induced by the operation has been a major concern. Based on our study, the possible impact of CO₂ pneumoperitoneum on immune disturbance and possible implantation metastasis could not be determined. However, previous studies have reported no significant increase in metastasis implantation after LARG, and the rate of incision metastasis did not differ between patients who underwent and those who did not undergo CO₂ pneumoperitoneum during surgery^[16]. Similarly, no implantation metastasis was found in patients treated with LARG in our study. We believe that gentle surgical maneuver without squeezing the tumor tissues, and withdrawal of the laparoscopic instruments only after the intra-abdominal gas is completely removed, are important.

In conclusion, LARG is a safe, effective, and minimally invasive approach for the treatment of gastric cancer. LARG may offer better short-term benefits to patients than ORG offers. Further studies are needed to investigate the long-term efficacy of the LARG approach.

COMMENTS

Background

Gastric cancer is one of the most common malignant tumors worldwide, with a yearly incidence of about 900000. Laparoscopic radical gastrectomy (LARG) has been increasingly used as a promising approach for the management of gastric cancer because of its minimal invasiveness and a potential to treat successfully patients with lymph node metastasis. Although LARG and laparoscopic D2 gastrectomy have now been widely used in the treatment of gastric cancer, including advanced gastric carcinoma, the short- and long-term benefits are unclear. The short-term outcomes of LARG have recently been reported, although these studies were based on small samples. In the current study, authors compared the short-term outcomes between LARG and open radical gastrectomy (ORG) performed in patients with gastric cancer in our department.

Research frontiers

LARG and laparoscopic D2 gastrectomy have now been widely used in the treatment of gastric cancer, including advanced gastric carcinoma. The research hotspot is how to investigate the short-term benefits of LARG and ORG in patients with gastric cancer.

Innovations and breakthroughs

Based on this study, authors believe that LARG is a safe, effective, and minimally invasive approach for the treatment of gastric cancer, as previously reported. The long-term efficacy of LARG in patients with gastric cancer has also been reported. In this long-term follow-up study, no significant difference in the 5-year survival rate was observed between 136 patients with gastric cancer who underwent LARG and 120 patients who underwent ORG. Well-exposed surgical fields could help reduce blood vessel damage and reduce intraoperative blood loss. A satisfactory surgical field can be obtained using laparoscopy with the assistance of an ultrasonic knife and titanium clips, and this could greatly reduce intraoperative blood loss. Currently, the same surgical processes used in traditional radical gastrectomy are still used in LARG, including blood vessel ligation at the origin, excessive margin resection, and removal of perigastric lymphoid tissues. However, because LARG is performed with laparoscopic instruments inside the abdominal cavity, mechanical organ damage by direct contact with the stomach during surgery can be minimized.

Applications

The results suggest that LARG is a safer, more effective, and less-invasive approach for treating gastric cancer with a better short-term efficacy.

Terminology

LARG: LARG is a novel minimally invasive surgical technique. It is associated with such advantages as less injury, reduced postoperative pain, lower impact on immune function, rapid recovery of gastrointestinal function, and short hospital stay.

Peer review

The authors have performed a well-designed study and submitted a full detailed manuscript. The overall body of the article is fine and they have presented the results and discussion well.

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