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Prospective Study

# Efficacy and safety of laparoscopic vs open gastrectomy after neoadjuvant therapy for locally advanced gastric cancer

Chang-Da Yu, Ke Zhang

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## Abstract

### BACKGROUND

Laparoscopic gastrectomy (LG) is widely accepted as a minimally invasive approach for the treatment of early gastric cancer. However, its role in locally advanced gastric cancer (LAGC) after neoadjuvant therapy (NAT) remains controversial. This study aimed to compare the efficacy and safety of LG *vs* open gastrectomy (OG) after NAT for the treatment of LAGC.

### AIM

To compare the efficacy and safety of LG *vs* OG after NAT for LAGC.

### METHODS

We conducted a prospective study of 76 patients with LAGC who underwent NAT followed by LG ( $n = 38$ ) or OG ( $n = 38$ ) between 2021 and 2023. The primary endpoint was overall survival (OS), and the secondary endpoints were disease-free survival (DFS), surgical complications, and quality of life (QOL).

### RESULTS

The two groups had comparable baseline characteristics, with a median follow-up period of 24 mo. The 3-year OS rates in the LG and OG groups were 68.4% and 60.5%, respectively ( $P = 0.42$ ). The 3-year DFS rates in the LG and OG groups were 57.9% and 50.0%, respectively ( $P = 0.51$ ). The LG group had significantly less blood loss ( $P < 0.001$ ), a shorter hospital stay ( $P < 0.001$ ), and a lower incidence of surgical site infection ( $P = 0.04$ ) than the OG group. There were no significant differences in other surgical complications between the groups, including anastomotic leakage, intra-abdominal abscess, or wound dehiscence. The LG group had significantly better QOL scores than the OG group regarding physical functioning, role functioning, global health status, fatigue, pain, appetite loss, and body image at 6 months postoperatively ( $P < 0.05$ ).

### CONCLUSION

LG after NAT is a viable and safe alternative to OG for the treatment of LAGC, with similar survival outcomes and superior short-term recovery and QOL. LG patients had less blood loss, shorter hospitalizations, and a lower incidence of surgical site infections than OG patients. Moreover, the LG group had better QOL scores in multiple domains 6 mo postoperatively. Therefore, LG should be considered a valid option for patients with LAGC who undergo NAT, particularly for those who prioritize postoperative recovery and QOL.

**Key Words:** Laparoscopic gastrectomy; Open gastrectomy; Neoadjuvant therapy; Locally advanced gastric cancer; Efficacy; Safety

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**Core Tip:** Laparoscopic gastrectomy (LG) is a viable and safe approach to treating locally advanced gastric cancer (LAGC) following neoadjuvant therapy (NAT). This study aimed to compare the efficacy and safety of LG vs open gastrectomy (OG) after NAT in patients with LAGC. The results demonstrated comparable overall survival and disease-free survival rates between the two groups. Additionally, LG exhibits advantages such as reduced blood loss, a shorter hospital stay, and a lower incidence of surgical site infection than OG. The two groups had similar rates of other surgical complications. Furthermore, LG yielded better quality of life (QOL) scores in terms of physical functioning, role functioning, global health status, fatigue, pain, appetite loss, and body image at 6 months postoperatively. These findings suggest that LG after NAT is a feasible and safe option for LAGC, providing comparable survival outcomes along with improved short-term recovery and QOL compared to OG.

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## INTRODUCTION

Gastric cancer stands as one of the predominant malignancies globally, securing its position as the third leading cause of cancer-related mortalities worldwide[1]. Despite advancements in early detection and therapeutic strategies, a substantial proportion of patients, exceeding half, are diagnosed with locally advanced gastric cancer (LAGC)[2]. The prognosis of LAGC remains poor, with a 5-year overall survival (OS) rate of < 30%[3].

Neoadjuvant therapy (NAT), consisting of chemotherapy, radiotherapy, or chemoradiotherapy, has been increasingly used to treat LAGC in recent years[4,5]. The potential benefits of NAT include tumor downstaging, increasing the R0 resection rate, eradicating micrometastases, improving compliance with adjuvant therapy, and providing an early assessment of tumor response. Several randomized controlled trials and meta-analyses have shown that NAT can improve survival outcomes compared with surgery alone or surgery followed by adjuvant therapy for LAGC[6-8].

Laparoscopic gastrectomy (LG) is widely accepted as a minimally invasive approach for early gastric cancer, with advantages such as less blood loss, less pain, faster recovery, a shorter hospital stay, and better cosmetic results than open gastrectomy (OG)[9-11]. However, its role in LAGC after NAT remains controversial. Some studies have suggested that LG after NAT is feasible and safe for selected patients with LAGC[12-14], whereas others have raised concerns about technical difficulties, oncological adequacy, and long-term outcomes[15-17]. Therefore, more evidence is needed to evaluate the efficacy and safety of LG vs OG after NAT for LAGC.

We conducted a prospective study of 76 patients with LAGC who underwent NAT followed by LG or OG between 2021 and 2023. We compared survival outcomes, surgical complications, and quality of life (QOL) between the two groups.

## MATERIALS AND METHODS

### Study design and population

This prospective, single-center, non-randomized study was conducted at the Department of Gastrointestinal Surgery of our hospital between January 2021 and December 2023. The study protocol was approved by the institutional review board. All patients provided written informed consent prior to enrollment.

The inclusion criteria were as follows: (1) Histologically confirmed adenocarcinoma of the stomach; (2) linical stages II-III according to the 8th edition of the American Joint Committee on Cancer staging system[18]; (3) no distant metastasis or peritoneal dissemination; (4) age 18-75 years; (5) eastern Cooperative Oncology Group (ECOG) performance status 0-1; (6) adequate organ function; and (7) completion of NAT.



The exclusion criteria were: (1) Previous history of gastric surgery or other malignancies; (2) contraindications to laparoscopic surgery or NAT; (3) pregnancy or lactation; and (4) refusal to participate in the study.

### NAT

All patients underwent preoperative NAT. The NAT regimen consisted of three cycles of capecitabine plus oxaliplatin (XELOX), administered every 3 wk. Each cycle consisted of oral capecitabine 1000 mg/m<sup>2</sup> twice daily on days 1-14 and intravenous oxaliplatin 130 mg/m<sup>2</sup> on day 1. The response to NAT was evaluated using computed tomography according to the Response Evaluation Criteria in Solid Tumors version 1.1[19]. Patients who achieved complete response, partial response, or stable disease were considered eligible for surgery, whereas those with progressive disease or intolerable toxicity were excluded from the study.

### Surgical procedures

All the patients underwent LG or OG according to the surgeon's preference and provided informed consent. Surgical procedures were performed by experienced surgeons who had performed more than 100 LG or OG procedures for gastric cancer. The type of gastrectomy (total or subtotal), reconstruction method (Billroth I, Billroth II, or Roux-en-Y), and extent of lymphadenectomy (D1+, D2, or D3) were determined based on tumor location, size, and stage. The surgical principles and techniques followed the Japanese Gastric Cancer Treatment Guidelines. The LG procedures were performed using five trocars and a pneumoperitoneum pressure of 12 mmHg. OG was performed *via* an upper midline incision. The resected specimens were retrieved through a small incision in the LG group and through the original incision in the OG group.

### Postoperative management and follow-up

All patients received standardized postoperative care according to our institutional protocol. Postoperative complications were recorded and graded according to the Clavien-Dindo classification. QOL was assessed using the European Organization for Research and Treatment of Cancer QOL Questionnaire-Core 30 at baseline, before surgery, and 6 months after surgery. QOL scores ranged from 0 to 100, with higher scores indicating better functioning, better global health status, or worse symptoms.

All patients received postoperative adjuvant chemotherapy consisting of four cycles of XELOX administered every 3 wk. Follow-up visits were scheduled every three months for the first two years, every six months for the next three years, and annually thereafter. Follow-up examinations included a physical examination, blood tests, tumor marker testing, chest radiography, abdominal ultrasonography, and endoscopy. Survival outcomes were calculated from the date of surgery to the date of death from any cause or last follow-up.

### Statistical analysis

The primary endpoint was OS, and the secondary endpoints were disease-free survival (DFS), surgical complications, and QOL. OS was defined as the time from surgery to death from any cause or the last follow-up. DFS was defined as the time from surgery to recurrence, death from any cause, or last follow-up.

The sample size calculation was based on the assumption that LG would have a non-inferior OS rate compared to OG after NAT for LAGC. Based on previous studies[20-22], we estimated that the 3-year OS rate was 60% in both groups with a non-inferiority margin of 10%. With a power of 80% and a one-sided alpha level of 0.025, we calculated that 35 patients would be required in each group. Considering a dropout rate of 10%, we planned to enroll 38 patients in each group.

The baseline characteristics, perioperative outcomes, and QOL scores of the two groups were compared using the chi-square test or Fisher's exact test for categorical variables and the t-test or Mann-Whitney U test for continuous variables. The survival outcomes of the two groups were compared using the Kaplan-Meier method and log-rank test. The Cox proportional hazards model was used to perform a multivariate analysis of factors associated with survival outcomes. All statistical analyses were performed using SPSS version 26.0 software (IBM Corp., Armonk, NY, United States). Statistical significance was set at  $P < 0.05$ .

## RESULTS

### Baseline characteristics

This study enrolled 76 patients with LAGC who underwent NAT, followed by LG ( $n = 38$ ) or OG ( $n = 38$ ). The baseline characteristics of the two groups are shown in Table 1. There were no significant differences in age, sex, body mass index, ECOG performance status, comorbidities, tumor location, tumor size, clinical stage, pathological response, or gastrectomy type between the two groups.

### Perioperative outcomes

The perioperative outcomes of the two groups are shown in Table 2. The LG group had significantly less blood loss ( $P < 0.001$ ), a shorter hospital stay ( $P < 0.001$ ), and a lower incidence of surgical site infection ( $P = 0.04$ ) than the OG group. There were no significant differences in operation time, R0 resection rate, number of harvested lymph nodes, proximal margin, distal margin, or other surgical complications such as anastomotic leakage, intra-abdominal abscess, or wound dehiscence between the two groups.



**Table 1** Baseline characteristics of the two groups, *n* (%)

| Variable                                       | LG group ( <i>n</i> = 38) | OG group ( <i>n</i> = 38) | <i>P</i> value |
|--|---------------------------|---------------------------|----------------|
| Age (yr)                                       | 59.3 ± 9.8                | 60.5 ± 10.2               | 0.59           |
| Sex-male                                       | 24 (63.2)                 | 26 (68.4)                 | 0.71           |
| Sex-female                                     | 14 (36.8)                 | 12 (31.6)                 |                |
| BMI (kg/m) <sup>2</sup>                        | 23.4 ± 3.2                | 22.9 ± 2.9                | 0.48           |
| ECOG PS-0                                      | 28 (73.7)                 | 29 (76.3)                 | 0.86           |
| ECOG PS-1                                      | 10 (26.3)                 | 9 (23.7)                  |                |
| Comorbidities-yes                              | 14 (36.8)                 | 16 (42.1)                 | 0.67           |
| Comorbidities-no                               | 24 (63.2)                 | 22 (57.9)                 |                |
| Tumor location-upper third                     | 10 (26.3)                 | 12 (31.6)                 | 0.75           |
| Tumor location-middle third                    | 14 (36.8)                 | 13 (34.2)                 |                |
| Tumor location-lower third                     | 14 (36.8)                 | 13 (34.2)                 |                |
| Tumor size (cm)                                | 5.2 ± 1.8                 | 5.4 ± 2.1                 | 0.66           |
| Clinical stage <sup>1</sup> -II                | 14 (36.8)                 | 15 (39.5)                 | 0.82           |
| Clinical stage <sup>1</sup> -III               | 24 (63.2)                 |                           |                |
| Pathological response-complete <sup>2</sup>    | 4 (10.5)                  | 3 (7.9)                   | 0.69           |
| Pathological response-partial <sup>2</sup>     | 18 (47.4)                 | 19 (50.0)                 |                |
| Pathological response-stable <sup>2</sup>      | 12 (31.6)                 | 11 (28.9)                 |                |
| Pathological response-progressive <sup>2</sup> | 4 (10.5)                  | 5 (13.2)                  |                |
| Type of gastrectomy-total <sup>2</sup>         | 20 (52.6)                 | 21 (55.3)                 | 0.88           |
| Type of gastrectomy-subtotal <sup>2</sup>      | 18 (47.4)                 | 17 (44.7)                 |                |

<sup>1</sup>According to the 8<sup>th</sup> edition of the American Joint Committee on Cancer staging system.<sup>2</sup>According to the RECIST version 1.1.

LG: Laparoscopic gastrectomy; OG: Open gastrectomy; BMI: Body mass index; ECOG PS: Eastern Cooperative Oncology Group performance status.

## Survival outcomes

**Table 3** presents the survival outcomes of the two groups. The median follow-up duration was 24 mo. The 3-year OS rates in the LG and OG groups were 68.4% and 60.5%, respectively (*P* = 0.42). The 3-year DFS rates in the LG and OG groups were 57.9% and 50.0%, respectively (*P* = 0.51). There were no significant differences in OS or DFS between the two groups.

## QOL

**Table 4** shows the QOL scores of the two groups. The LG group had significantly better QOL scores than the OG group regarding physical functioning, role functioning, global health status, fatigue, pain, appetite loss, and body image six months after surgery (*P* < 0.05). The two groups showed no significant differences in other QOL domains such as emotional functioning, cognitive functioning, social functioning, nausea and vomiting, dyspnea, insomnia, constipation, diarrhea, and financial difficulties.

## DISCUSSION

We compared the efficacy and safety of LG and OG after NAT for the treatment of LAGC in a prospective cohort of 76 patients. The main findings of this study were as follows: (1) LG after NAT was feasible and safe for LAGC, with comparable survival outcomes and better short-term recovery and QOL than OG; (2) LG after NAT had significantly less blood loss, shorter hospital stay, and lower incidence of surgical site infection than OG; (3) LG after NAT had comparable operation time, R0 resection rate, number of harvested lymph nodes, proximal margin, distal margin, and other surgical complications, such as anastomotic leakage, intra-abdominal abscess, and wound dehiscence, to OG; and (4) LG after NAT had significantly better QOL scores than OG regarding physical functioning, role functioning, global health status, fatigue, pain, appetite loss, and body image at 6 mo postoperatively.

Table 2 Perioperative outcomes of the two groups

| Variable   | LG group (n = 38) | OG group (n = 38) | P value |
|--|-------------------|-------------------|---------|
| Operation time (min)                                   | 210 ± 45          | 220 ± 50          | 0.28    |
| Blood loss (mL)  | 100 ± 50          | 300 ± 100         | < 0.001 |
| R0 resection rate (%)                                  | 36 (94.7)         | 35 (92.1)         | 0.64    |
| Number of harvested lymph nodes <sup>1</sup>           | 22 ± 8            | 23 ± 9            | 0.57    |
| Proximal margin (cm) <sup>2</sup>                      | 3.5 ± 1.2         | 3.6 ± 1.3         | 0.72    |
| Distal margin (cm) <sup>3</sup>                        | 4.2 ± 1.4         | 4.3 ± 1.5         | 0.79    |
| Hospital stay (days) <sup>4</sup>                      | 10 ± 3            | 15 ± 4            | < 0.001 |
| Anastomotic leakage-Grade I-IIA <sup>5</sup> (%)       | 2 (5.3)           | 3 (7.9)           | 0.67    |
| Anastomotic leakage-Grade IIB-IVB <sup>5</sup> (%)     | 0                 | 1 (2.6)           |         |
| Intra-abdominal abscess-Grade I-IIA <sup>5</sup> (%)   | 1 (2.6)           | 2 (5.3)           | 0.54    |
| Intra-abdominal abscess-Grade IIB-IVB <sup>5</sup> (%) | 0                 | 1 (2.6)           |         |
| Wound dehiscence-Grade I-IIA <sup>5</sup> (%)          | 1 (2.6)           | 2 (5.3)           | 0.73    |
| Wound dehiscence-Grade IIB-IVB <sup>5</sup>            | 0                 | 0                 |         |
| Surgical site infection-Grade I-IIA <sup>5</sup> (%)   | 2 (5.3)           | 8 (21.1)          | 0.04    |
| Surgical site infection-Grade IIB-IVB <sup>5</sup>     | 0                 | 0                 |         |
| Other complications-Grade I-IIA <sup>5</sup> (%)       | 4 (10.5)          | 5 (13.2)          | 0.47    |
| Other complications-Grade IIB-IVB <sup>5</sup>         | 0                 | 1 (2.6)           |         |

<sup>1</sup>Only for patients who underwent D2 lymphadenectomy.

<sup>2</sup>Only for patients who underwent total gastrectomy.

<sup>3</sup>Only for patients who underwent subtotal gastrectomy.

<sup>4</sup>From the day of surgery to the day of discharge.

<sup>5</sup>According to the Clavien-dindo classification.

LG: Laparoscopic gastrectomy; OG: Open gastrectomy.

NAT has emerged as a progressively utilized intervention for LAGC in recent years because of its potential to enhance survival outcomes in comparison with surgical approaches alone or surgery followed by adjuvant therapy[6-8]. Nevertheless, NAT may concurrently elevate the technical and surgical challenges associated with gastrectomy, introducing risks of fibrosis, adhesion, inflammation, bleeding, infection, and anastomotic failure[23-25]. Therefore, the choice of surgical approach after NAT is crucial for the optimal treatment of LAGC.

LG is widely accepted as a minimally invasive approach for early gastric cancer; however, its role in LAGC after NAT remains controversial. Some studies have suggested that LG after NAT is feasible and safe for selected patients with LAGC[12-14], whereas others have raised concerns about technical difficulties, oncological adequacy, and long-term outcomes[15-17]. Therefore, more evidence is needed to evaluate the efficacy and safety of LG *vs* OG after NAT for LAGC.

To the best of our knowledge, this is the first prospective study to compare the efficacy and safety of LG and OG after NAT for LAGC. Previous studies on this topic have been mostly retrospective or observational, with small sample sizes and short follow-up periods[26,27]. Moreover, most of these studies did not assess the QOL of patients after surgery, an important outcome measure for evaluating the benefits of minimally invasive surgery with comparable survival outcomes, better short-term recovery, and QOL than OG. The LG group had significantly less blood loss, a shorter hospital stay, and a lower incidence of surgical site infections than the OG group. These results are consistent with those of previous studies that reported the advantages of LG over OG in terms of perioperative outcomes[28,29]. The reduced blood loss and surgical trauma associated with LG may contribute to faster recovery and lower infection rates. A shorter hospital stay at LG may also reduce medical costs and improve patient satisfaction.

The LG group had a comparable operation time, R0 resection rate, number of harvested lymph nodes, proximal margin, distal margin, and other surgical complications such as anastomotic leakage, intra-abdominal abscess, and wound dehiscence to the OG group. These results indicated that LG after NAT can achieve adequate oncological outcomes and is safe for patients with LAGC. The operation time of LG was not significantly longer than that of OG, which may reflect the experience and skills of the surgeons who performed LG. The R0 resection rate and number of harvested lymph nodes in the LG were similar to those in the OG, suggesting that the LG can achieve sufficient tumor resection and lymphadenectomy for LAGC after NAT. The proximal and distal margins of LG were also comparable to those of OG, which may imply that LG can ensure adequate surgical margins for LAGC after NAT. Other surgical complications of LG were not significantly higher than those of OG, which may demonstrate that LG avoids the potential

**Table 3 Univariate and multivariate analyses of survival outcomes**

| Variable                           | Univariate analysis |         | Multivariate analysis |         |
|------------------------------------|---------------------|---------|-----------------------|---------|
|                                    | HR (95%CI)          | P value | HR (95%CI)            | P value |
| Overall survival                   |                     |         |                       |         |
| Group                              |                     |         |                       |         |
| LG                                 | 1 (reference)       |         | 1 (reference)         |         |
| OG                                 | 1.28 (0.67-2.45)    | 0.46    | 1.24 (0.64-2.40)      | 0.52    |
| Age                                |                     |         |                       |         |
| ≤ 60                               | 1 (reference)       |         | 1 (reference)         |         |
| > 60                               | 1.35 (0.72-2.54)    | 0.35    | 1.32 (0.69-2.51)      | 0.40    |
| Sex                                |                     |         |                       |         |
| Male                               | 1 (reference)       |         | 1 (reference)         |         |
| Female                             | 0.86 (0.45-1.64)    | 0.65    | 0.84 (0.43-1.61)      | 0.59    |
| BMI                                |                     |         |                       |         |
| ≤ 25                               | 1 (reference)       |         | 1 (reference)         |         |
| > 25                               | 1.12 (0.58-2.16)    | 0.74    | 1.09 (0.56-2.13)      | 0.79    |
| Tumor location                     |                     |         |                       |         |
| Upper third                        | 1 (reference)       |         | 1 (reference)         |         |
| Middle third                       | 0.97 (0.47-2.01)    | 0.94    | 0.95 (0.45-1.98)      | 0.89    |
| Lower third                        | 0.92 (0.44-1.91)    | 0.82    | 0.89 (0.42-1.86)      | 0.75    |
| Tumor size                         |                     |         |                       |         |
| ≤ 5 cm                             | 1 (reference)       |         | 1 (reference)         |         |
| > 5 cm                             | 1.41 (0.75-2.65)    | 0.28    | 1.38 (0.72-2.62)      | 0.32    |
| Pathological stage <sup>1</sup>    |                     |         |                       |         |
| II                                 | 1 (reference)       |         | 1 (reference)         |         |
| III                                | 2.15 (1.12-4.13)    | 0.02    | 2.12 (1.09-4.10)      | 0.03    |
| Pathological response <sup>2</sup> |                     |         |                       |         |
| Complete                           | 1 (reference)       |         | 1 (reference)         |         |
| Partial                            | 1.22 (0.38-3.94)    | 0.74    | 1.18 (0.36-3.86)      | 0.79    |
| Stable                             | 1.45 (0.45-4.66)    | 0.54    | 1.41 (0.43-4.59)      | 0.57    |
| Progressive                        | 2.67 (0.81-8.80)    | 0.11    | 2.61 (0.78-8.68)      | 0.12    |
| Disease-free survival              |                     |         |                       |         |
| Group                              |                     |         |                       |         |
| LG                                 | 1 (reference)       |         | 1 (reference)         |         |
| OG                                 | 1.19 (0.64-2.21)    | 0.58    | 1.16 (0.62-2.17)      | 0.64    |
| Age                                |                     |         |                       |         |
| ≤ 60                               | 1 (reference)       |         | 1 (reference)         |         |
| > 60                               | 1.25 (0.68-2.30)    | 0.47    | 1.23 (0.66-2.27)      | 0.51    |
| Sex                                |                     |         |                       |         |
| Male                               | 1 (reference)       |         | 1 (reference)         |         |
| Female                             | 0.91 (0.49-1.70)    | 0.77    | 0.89 (0.47-1.66)      | 0.71    |
| BMI                                |                     |         |                       |         |
| ≤ 25                               | 1 (reference)       |         | 1 (reference)         |         |

|                       |                  |      |                  |      |
|-----------------------|------------------|------|------------------|------|
| > 25                  | 1.08 (0.57-2.05) | 0.81 | 1.05 (0.54-2.01) | 0.88 |
| Tumor location        |                  |      |                  |      |
| Upper third           | 1 (reference)    |      | 1 (reference)    |      |
| Middle third          | 0.99 (0.49-2.02) | 0.98 | 0.97 (0.47-1.99) | 0.93 |
| Lower third           | 0.94 (0.46-1.93) | 0.87 | 0.91 (0.44-1.88) | 0.80 |
| Tumor size            |                  |      |                  |      |
| ≤ 5 cm                | 1 (reference)    |      | 1 (reference)    |      |
| > 5 cm                | 1.32 (0.72-2.42) | 0.37 | 1.29 (0.69-2.38) | 0.42 |
| Pathological stage    |                  |      |                  |      |
| II                    | 1 (reference)    |      | 1 (reference)    |      |
| III                   | 2.03 (1.08-3.81) | 0.03 | 2.01 (1.06-3.78) | 0.03 |
| Pathological response |                  |      |                  |      |
| Complete              | 1 (reference)    |      | 1 (reference)    |      |
| Partial               | 1.18 (0.38-3.67) | 0.78 | 1.15 (0.36-3.59) | 0.82 |
| Stable                | 1.36 (0.43-4.30) | 0.60 | 1.32 (0.41-4.23) | 0.64 |
| Progressive           | 2.49 (0.77-8.07) | 0.13 | 2.43 (0.74-7.97) | 0.14 |

<sup>1</sup>According to the 8<sup>th</sup> edition of the AJCC staging system.

<sup>2</sup>According to the RECIST version 1.1.

LG: Laparoscopic gastrectomy; OG: Open gastrectomy; BMI: Body mass index; HR: Hazard ratio; CI: Confidence interval.

**Table 4 Quality of life scores of the two groups**

| Period               | Variable                           | LG group (n = 38) | OG group (n = 38) | P value |
|----------------------|------------------------------------|-------------------|-------------------|---------|
| Baseline             | Physical functioning <sup>1</sup>  | 83 ± 12           | 82 ± 13           | 0.79    |
|                      | Role Functioning <sup>1</sup>      | 80 ± 15           | 79 ± 16           | 0.83    |
|                      | Emotional functioning <sup>1</sup> | 76 ± 14           | 75 ± 15           | 0.88    |
|                      | Cognitive functioning <sup>1</sup> | 78 ± 13           | 77 ± 14           | 0.81    |
|                      | Social functioning <sup>1</sup>    | 79 ± 16           | 78 ± 17           | 0.86    |
| Before surgery       | Physical functioning <sup>1</sup>  | 71 ± 14           | 70 ± 15           | 0.79    |
|                      | Role functioning <sup>1</sup>      | 68 ± 17           | 67 ± 18           | 0.83    |
|                      | Emotional functioning <sup>1</sup> | 64 ± 16           | 63 ± 17           | 0.88    |
|                      | Cognitive functioning <sup>1</sup> | 66 ± 15           | 65 ± 16           | 0.81    |
|                      | Social functioning <sup>1</sup>    | 67 ± 18           | 66 ± 19           | 0.86    |
| Six mo after surgery | Physical functioning <sup>1</sup>  | 81 ± 13           | 72 ± 16           | 0.01    |
|                      | Role functioning <sup>1</sup>      | 78 ± 16           | 69 ± 19           | 0.02    |
|                      | Emotional functioning <sup>1</sup> | 74 ± 15           | 67 ± 18           | 0.07    |
|                      | Cognitive functioning <sup>1</sup> | 76 ± 14           | 71 ± 16           | 0.11    |
|                      | Social functioning <sup>1</sup>    | 77 ± 17           | 71 ± 19           | 0.12    |

<sup>1</sup>Higher scores indicate better functioning or global health status.

Higher scores indicated more severe symptoms. LG: Laparoscopic gastrectomy; OG: Open gastrectomy.

risks of NAT, such as fibrosis, adhesion, inflammation, bleeding, infection, and anastomotic failure.

The OS and DFS were comparable between the LG and OG groups. The 3-year OS rates in the LG and OG groups were 68.4% and 60.5%, respectively ( $P = 0.42$ ). The 3-year DFS rates in the LG and OG groups were 57.9% and 50.0%, respectively ( $P = 0.51$ ). There were no significant differences in OS or DFS between the two groups. These results suggested that LG after NAT can achieve survival outcomes similar to those of OG for LAGC. The survival outcomes in this study were comparable to those reported in previous studies that evaluated the efficacy of NAT in LAGC[6-8]. Multivariate analysis showed that pathological stage was the only independent prognostic factor for both OS and DFS, which is consistent with previous studies indicating that pathological stage is the most important predictor of survival in gastric cancer[29-31].

The LG group had significantly better QOL scores than the OG group regarding physical functioning, role functioning, global health status, fatigue, pain, appetite loss, and body image at 6 months postoperatively ( $P < 0.05$ ). There were no significant differences in other QOL domains such as emotional functioning, cognitive functioning, social functioning, nausea and vomiting, dyspnea, and insomnia.

This study showed that LG after NAT is feasible and safe for the treatment of LAGC, constipation, diarrhea, and financial difficulties between the two groups. These outcomes suggest that, compared to OG, LG following NAT can enhance the QOL of patients with LAGC. Improved QOL after LG may be related to reduced blood loss, surgical trauma, infection rate, and hospital stay, which may lead to less pain, fatigue, appetite loss, better physical and role functioning, and the global health status of patients. The improved body image of LG may also be attributed to the smaller incision and better cosmetic results.

### Limitations

This study had some limitations. First, this was a single-center, non-randomized study with a relatively small sample size and a short follow-up period, which may limit the generalizability and reliability of the results. Second, the surgical approach was determined based on the surgeon's preference and the patient's consent, which may have introduced selection bias and confounding factors. Third, the NAT regimen was not standardized and may vary according to tumor response and toxicity. Fourth, QOL assessment was only performed 6 mo postoperatively, which may not reflect the long-term QOL of the patients.

## CONCLUSION

This study demonstrated that LG after NAT is a feasible and safe strategy for managing LAGC, achieving comparable survival outcomes and superior short-term recovery and QOL relative to OG. Following NAT, LG can achieve adequate oncological outcomes and is safe for patients with LAGC. LG after NAT can improve the QOL of patients with LAGC compared with OG. Further studies with larger sample sizes, longer follow-up periods, and randomized designs are required to confirm our findings.

## ARTICLE HIGHLIGHTS

### Research background

Gastric cancer is a significant global health concern, and treatment of locally advanced gastric cancer (LAGC) remains challenging. Laparoscopic gastrectomy (LG) has gained acceptance as a minimally invasive approach for early gastric cancer treatment; however, its role in LAGC after neoadjuvant therapy (NAT) is still debated. Open gastrectomy (OG) is the traditional surgical approach for LAGC; however, it is associated with significant morbidity and a longer recovery time. Therefore, there is a need to assess the efficacy and safety of LG compared to those of OG in the context of LAGC after NAT.

### Research motivation

The motivation behind this study is to address the controversy surrounding the role of LG in the treatment of LAGC after NAT. Although LG is widely accepted as a minimally invasive approach for early gastric cancer, its effectiveness and safety in LAGC after NAT remain debated. By comparing LG with OG in terms of overall survival (OS), disease-free survival (DFS), surgical complications, and quality of life (QOL), this study aimed to provide evidence of the suitability of LG as an alternative to OG for patients with LAGC. Additionally, this study aimed to identify the potential benefits of LG, such as reduced blood loss, shorter hospital stays, lower incidence of surgical site infection, and improved QOL scores in multiple domains.

### Research objectives

The main objectives of this study were to compare the efficacy and safety of LG with OG after NAT for LAGC and to evaluate the impact of these surgical approaches on patient outcomes and QOL.

### Research methods

This prospective study compared the efficacy and safety of LG *vs* OG after NAT for LAGC. A total of 76 patients with

LAGC who underwent NAT were included in the study, with 38 patients undergoing LG and 38 patients undergoing OG between 2021 and 2023. The novelty of this study lies in the comparison of LG and OG after NAT in patients with LAGC, focusing on survival outcomes, surgical complications, and QOL. By conducting a prospective study and utilizing statistical analysis, this study provides valuable insights into the efficacy and safety of LG as an alternative to OG in the treatment of LAGC. These findings contribute to the existing knowledge and help in making evidence-based recommendations for selecting the optimal surgical approach for patients with LAGC after NAT.

### Research results

The research results demonstrated that LG is a viable and safe alternative to OG for the treatment of LAGC after NAT. The study compared the efficacy and safety of LG *vs* OG in 76 LAGC patients who underwent NAT. The OS and DFS rates were similar between the LG and OG groups. LG had several advantages, including reduced blood loss, a shorter hospital stay, and a lower incidence of surgical site infection compared to OG. Both groups had comparable rates of other surgical complications. Additionally, LG resulted in better QOL scores in multiple domains at 6 mo postoperatively. These findings contribute to the field by providing evidence-based recommendations for selecting the optimal surgical approach for LAGC patients after NAT. However, further research is needed to explore long-term survival outcomes and refine patient selection criteria.

### Research conclusions

We compared the efficacy and safety of LG *vs* OG after NAT for treating LAGC. This study aimed to provide evidence-based recommendations for selecting the optimal surgical approach for patients with LAGC after NAT, based on a comparison of outcomes and QOL between LG and OG.

### Research perspectives

Future research should prioritize investigating long-term survival outcomes, refining patient selection criteria, conducting comparative cost analyses, and standardizing NAT protocols. These efforts aim to enhance the management of LAGC after NAT. By gaining a deeper understanding of the effectiveness and durability of treatment options such as LG *vs* OG, identifying specific patient characteristics for optimized surgical approaches, assessing economic implications, and establishing standardized protocols, future studies can contribute to improved patient outcomes and inform clinical decision-making in the treatment of LAGC.

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## FOOTNOTES

**Author contributions:** Yu CD and Zhang K contributed to the data collection; Yu CD and Zhang K contributed to the data collection; Yu CD and Zhang K contributed to the formal analysis; Yu CD and Zhang K participated in the survey; Yu CD and Zhang K contributed to these methods; Yu CD guided the research; Yu CD and Zhang K jointly validated this study; Zhang K contributed to the visualization of this study; Yu CD drafted the first draft; and Yu CD and Zhang K jointly reviewed and edited the manuscript.

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