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Long-term outcomes of laparoscopic versus open total gastrectomy in patients with advanced gastric cancer after neoadjuvant chemotherapy: a retrospective cohort study

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Abstract

Background This study was conducted to investigate the long-term outcomes of laparoscopic total gastrectomy (LTG) versus open total gastrectomy (OTG) in patients with advanced gastric cancer (AGC) after neoadjuvant chemotherapy (NACT).

Methods Patients with AGC who received NACT before surgery were enrolled in either the LTG or OTG group. Propensity score matching (PSM) (1:2) was performed between the two groups based on the propensity score using a 0.15 calliper width. Three-year overall survival (OS) and disease-free survival (DFS) were compared between these two groups before and after PSM. OS and DFS rates were calculated by the Kaplan–Meier method, and any differences in survival were evaluated with a log-rank test. Univariate and multivariate Cox proportional hazards analyses were used to estimate the simultaneous effects of prognostic factors on survival and the hazard ratio (HR) between LTG and OTG patients.

Results A total of 144 patients completed the follow-up, with 24 patients in the LTG group and 120 patients in the OTG group. After a mean follow-up of 64.40 months, there were no significant differences in the 3-year OS or DFS rates between the two groups before ($P=0.453$ and $P=0.362$, respectively) or after PSM ($P=0.972$ and $P=0.884$, respectively). Multivariate Cox proportional hazards analysis indicated that ypN stage was an independent risk factor for worse OS ($P=0.013$).

Conclusions This study showed that LTG with D2 lymphadenectomy performed by an experienced surgical team resulted in comparable 3-year OS and DFS compared with OTG in patients with AGC after NACT.

Trial registration This study is not registered.

Keywords Long-term outcomes, Laparoscopic, Open, Total gastrectomy, Neoadjuvant chemotherapy

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Introduction

Gastric cancer (GC) is one of the most common malignant tumors worldwide [1]. In China, many new cases are diagnosed each year, with over 80% of these cases in advanced stages [2]. Currently, radical surgery is the most effective treatment for GC [3]. However, the treatment of AGC is still a major challenge because of the high recurrence rate and low initial R0 resection rate [4–6]. NACT has been widely accepted for the treatment of AGC based on the MAGIC, FFCD9703, FLOT4-AIO, and RESOLVE trials [7–10].

Since Kitano et al. performed the first laparoscopic distal gastrectomy (LDG) for GC in 1994 [11] and Azagra et al. reported the first laparoscopy-assisted total gastrectomy with lymph node dissection for GC in 1999 [12], this minimally invasive procedure has gradually become popular worldwide. Previous studies have suggested that laparoscopic gastrectomy, including LDG and LTG, has advantages over open gastrectomy in reducing injury, rapidly recovering gastrointestinal function postoperatively, decreasing postoperative pain, minimizing wound size, etc. [13, 14]. LDG has been recommended for the treatment of clinical stage I GC patients [15]. In addition, several randomized controlled trials (RCTs), including the CLASS01 [16–18], KLASS02 [19, 20], and JLSSG0901 studies [21, 22], have indicated that LDG has comparable safety and short- and long-term outcomes compared to open distal gastrectomy in the treatment of AGC. These advantages drive experts to explore a wider range of use for laparoscopic gastrectomy.

Recently, a European RCT indicated that LTG was not inferior to OTG in terms of the oncological quality of resection, postoperative complications, recovery, or one-year survival in Western patients with AGC after NACT [23]. Additionally, two retrospective studies reported that LTG had comparable long-term outcomes to OTG among patients with AGC after NACT [24, 25]. Although these studies reported long-term outcomes, solid evidence is still lacking regarding the long-term outcomes of LTG in patients with AGC after NACT.

Previously, we found that LTG had comparable perioperative safety and histological findings with less invasive and less intravenous patient-controlled analgesia (IV-PCA) use versus OTG after NACT [26]. Here, we conducted the present study to investigate long-term outcomes between LTG and OTG among patients with AGC after NACT.

Materials and methods

Study design and participants

AGC patients ($cT_{2\text{-}4a}N_{any}M_0$) who received 2–5 cycles of NACT before total gastrectomy were enrolled in the present study. In addition, patients aged between 18 and 80 years with a Karnofsky performance scale score higher than 70 were included. All enrolled patients were treated at Peking University Cancer Hospital and Institute Gastrointestinal Cancer Center from April 2013 to August 2018. Patients were excluded if they had other malignancies or had medical conditions requiring emergency surgeries. Approval was obtained from the Ethics Committee of Peking University Cancer Hospital and Institute (No. 2019YJZ26), and written informed consent was obtained from all patients or their relatives.

NACT treatment

The clinical stage at diagnosis, preoperative response assessment, NACT regimen, and intervention for adverse events were discussed by a multidisciplinary team (MDT). Enhanced abdominal computed tomography (CT) was used to evaluate the preoperative treatment response according to the Response Evaluation Criteria in Solid Tumors (RECIST version 1.1) [27]. All patients underwent CT scans for their baseline evaluation. The NACT regimens used in the present study were one-, two- or three-drug regimens based on the routine chemotherapy regimens for AGC.

Propensity score matching

Due to the unequal number of patients in each group and the significant difference in tumor size at baseline, a 1:2 ratio PSM using a 0.15 calliper width method was performed between the two groups. A multivariate logistic regression model was used to calculate propensity scores for each enrolled patient. The covariates selected for PSM included age, body mass index (BMI), sex, American Society of Anesthesiologists (ASA) score, tumor diameter, NACT regimen, and number of cycles of NACT. The present detailed procedures were the same as those described in a previous article published by our team [26].

Surgical techniques, postoperative complications, and postoperative adjuvant chemotherapy

The decision of whether to use an open or laparoscopic approach was also determined by the surgeon and patient together based on the tumor size and actual conditions of the patients. When a patient could not decide, the chief surgeon made the decision based on the above conditions. All patients in this study underwent standard total gastrectomy with D2 lymphadenectomy. Each patient underwent laparoscopic exploration before the operation. In addition, peritoneal lavage cytology was performed for all enrolled patients. The surgeon separated and tagged the lymph node as soon as the surgery was completed. Notably, the detailed surgical procedure has been described previously [26].

Postoperative complications were defined as complications during the postoperative hospital stay and were recorded following the Clavien–Dindo classification system. These details were also presented in our previously published articles [26].

Postoperative adjuvant chemotherapy and its regimens were also determined by the MDT according to the pathology results of the surgical resection specimens and patient tolerance to adjuvant chemotherapy.

End points

Patients were followed up for at least 36 months or until recurrence, death or loss to follow-up after surgery. OS was calculated from the date of surgery until the date of death (event) or the last follow-up (censored). DFS was calculated from the day of surgery until the day of recurrence or metastasis (event), the day of death from any cause (event), or the last follow-up (censored).

Statistical analysis

The Kaplan–Meier method was used to estimate OS and DFS between the groups at one, two, and three years, and any differences in survival were evaluated by the log-rank test. Cox proportional hazards regression analysis was used to estimate univariate and multivariate hazard ratios (HRs) for OS and DFS. All the statistical analyses were conducted with the SPSS package (SPSS v.24.0 software, IBM Corp., Armonk, NY, USA). Differences were considered to be statistically significant if the *P value was* < 0.05.

Results

Patient characteristics

First, 145 patients were enrolled in this study from April 2013 to August 2018. One patient in the OTG group was found to have peritoneal metastasis during the operation (ypM1) and was excluded from survival analysis. A total of 144 patients, with 24 patients in the LTG group and 120 patients in the OTG group, were analysed. Before PSM, there were significant differences in the long axis (3.33 ± 1.36 vs. 4.53 ± 2.56 cm, $P=0.028$) and short axis (2.58 ± 1.17 vs. 3.56 ± 2.29 cm, $P=0.045$) of the tumor between the LTG group and OTG group. Therefore, we used PSM to match factors that were significantly different between the LTG and OTG groups. The detailed characteristics of the patients before and after PSM are provided in Supplementary Table 1 and Supplementary Table 2, respectively.

After PSM, 15 patients (65.2%) in the LTG group and 39 patients (84.8%) in the OTG group received adjuvant chemotherapy. Additionally, adjuvant chemotherapy data were missing for six patients in the LTG group and seven patients in the OTG group. There was no statistically significant difference in the number of patients who received adjuvant chemotherapy between the two groups ($P=0.076$). The results of adjuvant chemotherapy are presented in Supplementary Table 4.

Overall survival (OS)

The mean follow-up period was 64.40 months (95% CI, 60.62–68.18 months). During the follow-up period, there were six deaths in the LTG group and 49 deaths in the OTG group. In the LTG group, all six patients died of cancer. In the OTG group, one patient died in a car accident, and the other 48 patients died of cancer. The OS rates were 87.5% and 94.2% at one year in the LTG group and the OTG group, respectively. The three-year OS rates were 75.0% in the LTG group and 73.3% in the OTG group. The mean OS of patients in the LTG group was 68.83 months (95% CI, 56.13–81.53 months), and that of patients in the OTG group was 69.40 months (95% CI, 62.69–76.11 months); there were no differences before ($P=0.453$; Fig. 1a) or after PSM ($P=0.972$; Fig. 1b). The OS curves are presented in Fig. 1. Univariate Cox proportional hazards regression analysis revealed that female sex (HR, 1.960; 95% CI 1.047–3.668, $P=0.032$), long axis diameter (HR, 1.099; 95% CI 1.002–1.206, $P=0.044$), short axis diameter (HR, 1.125; 95% CI 1.024–1.236, $P=0.014$), ypT stage ($P=0.002$), ypN stage ($P<0.001$), and blood vessel invasion ($P<0.001$) were significantly associated with OS. The details are presented in Table 1. Correlation analysis among sex, blood vessel invasion, tumor long axis, tumor short axis, ypT stage, and ypN stage revealed that sex was correlated with blood vessel invasion ($P=0.031$; Supplementary Table 3). Multivariate analysis with a Cox proportional hazards regression model showed that ypN stage was associated with OS ($P=0.013$). The results are provided in Table 2. In addition, univariate Cox regression analysis of patients after PSM revealed no significant difference in OS (HR, 0.983; 95% CI 0.373–2.592, $P=0.972$; Table 3).

Recurrence and disease-free survival (DFS)

There were six recurrence cases in the LTG group and 48 recurrence cases in the OTG group. The one-year DFS rates were 87.5% in the LTG group and 88.3% in the OTG group. LTG had a three-year DFS of 75.0%, and OTG had a three-year DFS of 69.2%. The mean DFS times in the LTG group were 68.71 months (95% CI, 55.93–81.49 months) and 67.74 months (95% CI, 60.64–74.85 months) in the OTG group, respectively, with no differences before ($P=0.362$; Fig. 1c) or after PSM ($P=0.884$; Fig. 1d). Univariate Cox proportional hazards regression analysis revealed that long-axis diameter (HR, 1.124, 95% CI 1.024–1.234, $P=0.014$), short-axis diameter (HR, 1.151; 95% CI 1.048–1.266, $P=0.003$), ypT stage ($P=0.001$), ypN stage ($P<0.001$), and blood vessel invasion ($P<0.001$) were

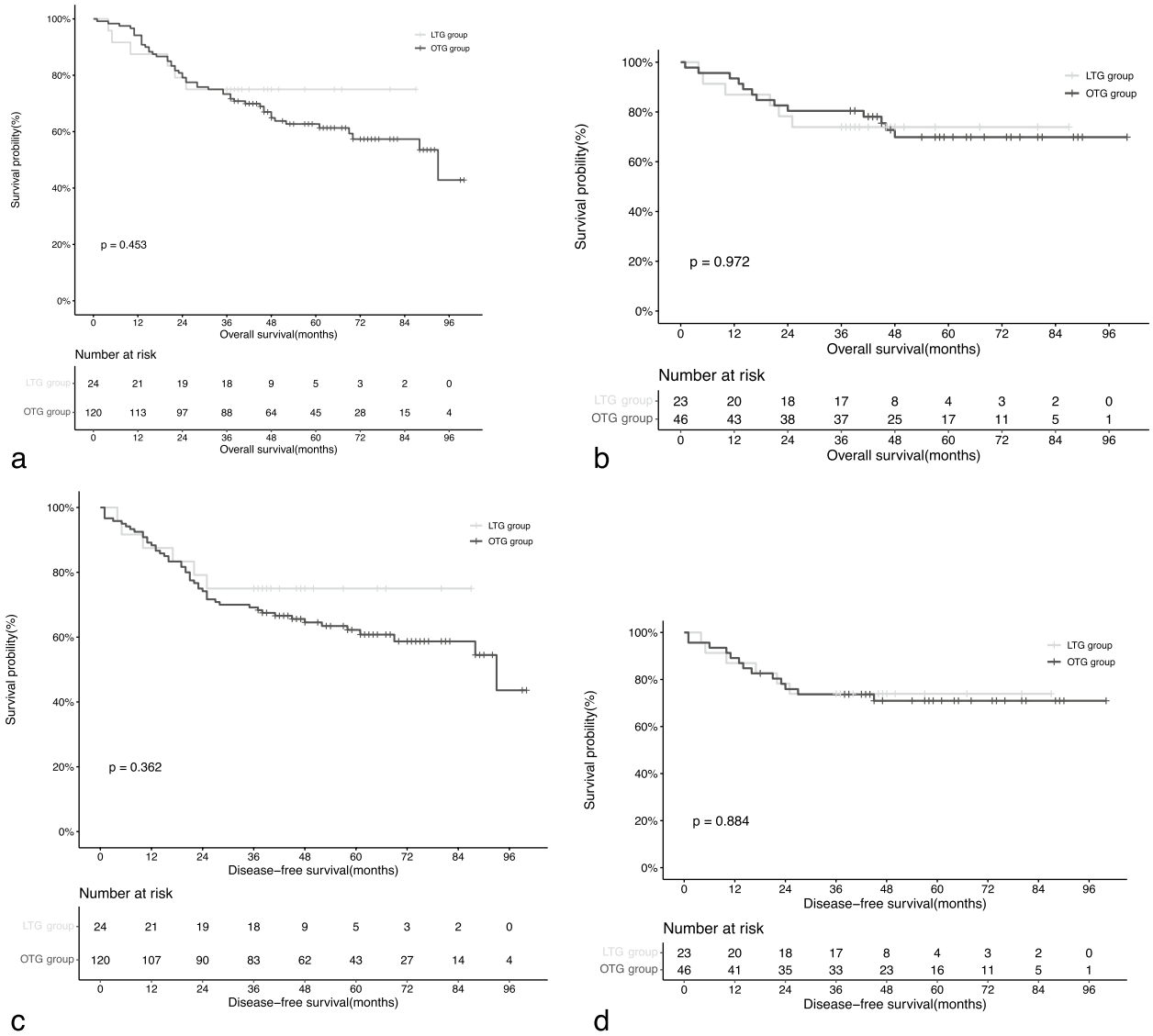

Fig. 1 OS and DFS curve before and after PSM between the LTG group and OTG group. **a** OS curve before PSM between the LTG group and OTG group. **b** OS curve after PSM between the LTG group and OTG group. **c** DFS curve before PSM between the LTG group and OTG group. **d** DFS curve after PSM between the LTG group and OTG group

significantly associated with DFS. The results are presented in Table 4. According to the multivariate Cox proportional hazards regression analysis, ypN stage was significantly associated with DFS ($P<0.007$; Table 5). Univariate Cox regression analysis of DFS in patients after PSM revealed no significant difference between the surgical approaches (HR, 1.074; 95% CI 0.408–2.828, $P=0.885$; Table 6).

Discussion

In this study, we found that the OS and DFS of LTG patients who underwent D2 lymphadenectomy for AGC after NACT were comparable to those of OTG patients who underwent surgery performed by experienced surgeons at three years postoperatively before and after adjusting for baseline data through PSM. Although several articles have reported the survival results of LTG for AGC after NACT [23–25], there is still a lack of sufficient robust evidence concerning the long-term survival of LTG versus OTG for AGC after NACT. This finding provides further evidence for the survival of patients treated with LTG for AGC after NACT.

Although the CLASS-02 multicenter RCT showed that there was no significant difference in the overall perioperative morbidity or mortality rates between the LTG and

Table 1 Univariate analysis Cox-regression analyses of the OS in patients

Variable	Hazard ratio, HR	95.0% CI for HR		*P-value*
		Lower	Upper	
Surgical approach				0.455
LTG	Ref			
OTG	1.382	0.589	3.239	0.457
Age				0.634
< 65	Ref			
≥ 65	1.141	0.663	1.964	0.634
Sex				0.032
Male	Ref			
Female	1.960	1.047	3.668	0.035
BMI				0.491
< 18.5	Ref			
18.5–24	0.946	0.226	3.970	0.940
≥ 24	0.684	0.160	2.915	0.607
Diameter in long axis	1.099	1.002	1.206	0.044
Diameter in short axis	1.125	1.024	1.236	0.014
ASA				0.890
1	Ref			
2	1.619	0.223	11.755	0.634
3	1.582	0.194	12.902	0.668
NACT Regimens				0.616
Platin-based	Ref			
Taxol-based	1.481	0.630	3.484	0.368
Others	1.277	0.457	3.571	0.641
Number of lymph nodes retrieved	1.008	0.987	1.030	0.456
Comorbidity				0.486
No	Ref			
Yes	1.220	0.697	2.136	0.487
Postoperative complications				0.226
No	Ref			
Yes	0.666	0.343	1.292	0.229
Lymph node dissection				0.703
D1 +	Ref			
D2	0.701	0.170	2.891	0.623
D2 +	0.978	0.189	5.053	0.979
Combined organ resection				0.848
No	Ref			
Yes	0.825	0.114	5.970	0.848
ypT stage				0.002
T0-1	Ref			
T2	1.943	0.325	11.631	0.467
T3	5.695	1.360	23.838	0.017
T4	8.232	1.908	35.503	0.005
ypN stage				< 0.001
N0	Ref			
N1	2.796	1.186	6.592	0.019
N2	2.948	1.334	6.514	0.008
N3	5.448	2.577	11.517	< 0.001
Blood vessel invasion				< 0.001

Table 1 (continued)

Variable	Hazard ratio, HR	95.0% CI for HR		*P-value*
		Lower	Upper	
No	Ref			
Yes	2.684	1.541	4.677	< 0.001
Borrmann type				0.494
I	Ref			
II	1.280	0.154	10.643	0.819
III	1.713	0.235	12.488	0.595
IV	2.671	0.334	21.366	0.354

Table 2 Multivariate Cox-regression analysis of the OS in patients

Variable	HR	95%CI	*P-value*
ypN stage			0.013
N0	Ref		
N1	2.480	1.011–6.088	0.047
N2	2.374	1.030–5.472	0.042
N3	3.698	1.610–8.491	0.002

Table 3 Univariate Cox-regression analysis results of OS in patients after PSM

Variable	HR	95%CI	*P-value*
Surgical approach			0.972
LTG	Ref		
OTG	0.983	0.373–2.592	0.972

OTG groups [28], long-term outcomes are lacking. This study revealed comparable long-term outcomes between LTG and OTG for AGC after NACT. These comparable survival results combined with the advantages in short-term outcomes reported by our center [26] suggested that LTG could be an alternative option for the treatment of AGC after NACT. Of course, further multicenter, high-quality RCTs with longer-term results and larger sample sizes are needed.

Compared with open surgery, laparoscopy can provide a magnified view and better exposure. However, laparoscopic manipulation and pneumoperitoneum effects might increase the risk of peritoneal dissemination, particularly for tumors with serosal invasion, free tumor cells in the intra-abdominal cavity, and positive lymph node metastasis, which potentially results in an increased risk of recurrence [20, 29]. However, our present study showed that the three-year DFS rates were 74.6% in the LTG group and 68.3% in the OTG group. The mean DFS was 68.43 months in the LTG group and 66.02 months in the OTG group, with no differences ($p = 0.393$). The present study demonstrated that LTG did not increase the risk of recurrence and did not decrease the DFS among patients with AGC after NACT compared to OTG.

NACT, a novel therapeutic paradigm for AGC, has been widely used due to its potential survival benefit in patients with GC [30, 31]. Additionally, the RESOLVE study showed that, compared with adjuvant-CapeOx, perioperative SOX had a clinically meaningful improvement in three-year DFS in patients with AGC who underwent D2 gastrectomy, but overall survival had not yet been reached [10]. For patients with advanced proximal gastric cancer without NACT, a recently published nonrandomized clinical trial revealed that the 3-year OS rate of LTG combined with spleen-preserving hilar lymphadenectomy was 79.1%, and among those with No. 10 lymph node metastasis who received adjuvant chemotherapy, the 3-year OS rate was 71.4% [32]. In the present study, the 3-year OS rate in the LTG group was 74.6%, which was similar to that in a previously published study. Although this study did not focus mainly on the effect of NACT on gastrectomy, it also showed that NACT was not inferior to surgery alone or adjuvant chemotherapy among patients with AGC after LTG. This study also provides a reference for the application of NACT for AGC patients who need total gastrectomy.

The STOMACH trial revealed that 85.5% of patients in the LTG group and 90.4% of patients in the OTG group were alive 1 year after surgery ($P = 0.701$) [23]. Additionally, Cui, Hao et al. [25] reported that the 3-year OS rates were 60.6% and 64.6% in the LTG and OTG groups, respectively, among AGC patients who received NACT in China, with no significant difference. They also found that the 3-year DFS rates were 54.5% and 51.8% in the LTG and OTG groups, respectively, with no significant difference [25]. The three-year OS rates were 75.0% and 73.3%, and the three-year DFS

Table 4 Univariate Cox-regression analyses of the DFS in patients

Variable	Hazard ratio, HR	95.0% CI for HR		*P-value*
		Lower	Upper	
Surgical approach				0.344
LTG	Ref			
OTG	1.504	0.642	3.525	0.348
Age				0.519
< 65	Ref			
≥ 65	1.195	0.694	2.058	0.520
Sex				0.057
Male	Ref			
Female	1.823	0.974	3.411	0.061
BMI				0.518
< 18.5	Ref			
18.5–24	1.030	0.246	4.319	0.968
≥ 24	0.749	0.176	3.190	0.696
Diameter in long axis	1.124	1.024	1.234	0.014
Diameter in short axis	1.151	1.048	1.266	0.003
ASA				0.847
1	Ref			
2	1.712	0.236	12.424	0.595
3	1.556	0.191	12.697	0.680
NACT Regimens				0.685
Platin-based	Ref			
Taxol-based	1.432	0.609	3.369	0.410
Others	1.199	0.428	3.358	0.730
Number of lymph nodes retrieved	1.009	0.988	1.031	0.412
Comorbidity				0.480
No	Ref			
Yes	1.224	0.699	2.143	0.480
Postoperative complications				0.180
No	Ref			
Yes	0.638	0.329	1.237	0.183
Lymph node dissection				0.741
D1 +	Ref			
D2	0.718	0.174	2.960	0.647
D2 +	0.975	0.189	5.035	0.976
Combined organ resection				0.812
No	Ref			
Yes	0.787	0.109	5.700	0.813
ypT stage				0.001
T0-1	Ref			
T2	1.889	0.316	11.310	0.486
T3	5.779	1.380	24.196	0.016
T4	8.520	1.974	36.770	0.004
ypN stage				< 0.001
N0	Ref			
N1	2.992	1.270	7.051	0.012
N2	2.795	1.262	6.190	0.011
N3	5.924	2.802	12.528	< 0.001
Blood vessel invasion				< 0.001

Table 4 (continued)

Variable	Hazard ratio, HR	95.0% CI for HR		*P-value*
		Lower	Upper	
No	Ref			
Yes	2.649	1.520	4.615	0.001
Borrmann type				0.432
I	Ref			
II	1.295	0.156	10.768	0.811
III	1.788	0.245	13.038	0.566
IV	2.854	0.357	22.827	0.323

Table 5 Multivariate Cox-regression analysis of the DFS in patients

Variable	HR	95%CI	*P-value*
ypN stage			0.007
N0	Ref		
N1	2.719	1.111–6.653	0.028
N2	2.228	0.966–5.138	0.060
N3	4.068	1.754–9.434	0.001

Table 6 Univariate Cox-regression analysis results of DFS in patients after PSM

Variable	HR	95%CI	*P-value*
Surgical approach			0.885
LTG	Ref		
OTG	1.074	0.408–2.828	0.885

rates were 75.0% and 69.2% in the LTG group and the OTG group, respectively. This study also indicated that there was no difference in three-year OS or three-year DFS between the LTG group and the OTG group in China for patients with AGC after NACT. However, in contrast to a previous study [25], the present study showed that LTG patients had a slightly greater three-year OS rate than did OTG patients among AGC patients after NACT in China.

Multivariate Cox proportional hazards regression analysis revealed that ypN stage was an independent risk factor for OS and DFS. A previous study suggested that the number of metastatic lymph nodes might lead to a high incidence of locoregional or peritoneal recurrence, which provided evidence that N stage is a prognostic factor for survival [33, 34]. We found that there were significant differences in tumor diameters on the long and short axes between the two groups at baseline. To minimize the impact of latent selection bias, 1:2 matching was performed between the LTG and OTG groups based on the propensity score. No significant differences were observed between the two groups after matching. The results of univariate Cox proportional hazards regression analysis after matching also indicated that LTG was not associated with long-term survival among patients with AGC after NACT. Both these results and the multivariate Cox proportional hazards regression results demonstrated that the surgical approach was not a risk factor for prognosis, and LTG after NACT had comparable long-term outcomes to OTG after NACT.

The present study has several limitations. Firstly, research on quality of life is indeed crucial, however, regrettably, we did not collect data on QoL in this study. Park et al. reported that TLTG significantly reduced grade I pulmonary complications (0.5% vs. 5.4%, $P=0.007$) and provided better QoL in dysphagia, pain, eating, odynophagia than LATG for patients with clinical stage I gastric cancer [35]. Thus, the difference in quality of life between TLTG and OTG is thought to be greater. Therefore, if the chemotherapy had been the same, there may have been a difference in quality of life between LTG and OTG group, because of surgery itself [35]. And future study should consider the QoL, when comparing LTG and OTG group. Secondly, this was a cohort study instead of a randomized controlled trial; although we performed PSM, there might also be potential confounders that were not eliminated. Second, this was a single-center retrospective study, in which selection bias and information bias caused by missing data, such as adjuvant chemotherapy data, were inevitable. Finally, the clinical tumor stages of the enrolled patients, which could influence the prognosis, were not recorded in the study. This might have an impact on the results.

Conclusion

This study revealed no significant differences in the three-year OS or three-year DFS between patients with AGC after NACT treated with LTG and those treated with OTG. LTG could be regarded as an alternative option for AGC patients after NACT with comparable long-term survival outcomes.

Abbreviations

LTG	Laparoscopic total gastrectomy
OTG	Open total gastrectomy
AGC	Advanced gastric cancer
NACT	Neoadjuvant chemotherapy
PSM	Propensity score matching
OS	Overall survival
DFS	Disease-free survival
HR	Hazard ratio
GC	Gastric cancer
LDG	Laparoscopic distal gastrectomy
RCTs	Randomized controlled trials
IV-PCA	Intravenous patient-controlled analgesia
MDT	Multidisciplinary team
CT	Computed tomography
RECIST	Response Evaluation Criteria in Solid Tumors
BMI	Body mass index
ASA	American Society of Anesthesiologists

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12669-w.

Supplementary Material 1.

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Authors' contributions
(I) Conception and design: Yinkui Wang, Zhemin Li, Ziyu Li; (II) Administrative support: Ziyu Li, Jiafu Ji; (III) Provision of study materials or patients: Xiaokang Lei, Yinkui Wang, Fei Shan; (IV) Collection and assembly of data: Xiaokang Lei, Shuangxi Li, Yongning Jia, Rulin Miao, Kan Xue; (V) Data analysis and interpretation: Xiaokang Lei, Yinkui Wang, Fei Shan, Zhemin Li, Jiafu Ji, Ziyu Li.; (VI) Manuscript writing: Yinkui Wang, Xiaokang Lei, Fei Shan, Shuangxi Li, Yongning Jia, Rulin Miao, Kan Xue, Zhemin Li, Jiafu Ji, Ziyu Li.; (VII) Final approval of manuscript: Yinkui Wang, Xiaokang Lei, Fei Shan, Shuangxi Li, Yongning Jia, Rulin Miao, Kan Xue, Zhemin Li, Jiafu Ji, Ziyu Li.
Yinkui Wang and Xiaokang Lei contributed equally to this work.

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Availability of data and materials
The datasets analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Approval was obtained from the Ethics Committee of Peking University Cancer Hospital and Institute (No. 2019YJZ26). Written informed consent was obtained from all patients or their relatives.

Consent for publication
Written informed consent was obtained from all patients or their relatives for publication.

Competing interests
The authors declare no competing interests.

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