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ORIGINAL ARTICLE

Feasibility of laparoscopic total gastrectomy for advanced Siewert type II and type III esophagogastric junction carcinoma: A propensity score-matched case-control study

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KEYWORDS
Gastric cancer;
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Summary *Objective:* This study aims to compare laparoscopic total gastrectomy (LTG) with open total gastrectomy (OTG) for treating advanced Siewert type II and type III adenocarcinoma of esophagogastric junction (AEG).
Methods: The data for this study included 872 patients with advanced Siewert type II and type III AEG who were candidates for undergoing total gastrectomy from January 2012 to December 2017 in Gastrointestinal Surgery Department of the First Hospital of Jilin University. After screening all the patients' data, 722 patients underwent the propensity score match (PSM) and out of them, 685 patients were selected and grouped into LTG group ($n = 468$) and OTG group ($n = 217$).
Results: Observing the patients' C reactive protein (CRP) level ($p < 0.001$) and pain score on postoperative day (POD) 1 ($p < 0.001$) and POD2 ($p < 0.001$) showed that the patients in LTG group were less stressed than those in OTG group. Moreover, patients who underwent LTG were able to sooner take liquid food ($p < 0.001$), get off beds to walk ($p < 0.001$), restore bowel function ($p < 0.001$), and had shorter postoperative stay ($p < 0.001$). On the other hand, these two groups showed no significant difference regarding postoperative complication rate ($p = 0.19$). The median survival for the LTG and OTG groups was 56 months and 47 months, respectively, and the 5-year overall survival (OS) was 40% and 29.1%, respectively. The LTG group obtained better OS ($p < 0.01$), with hazard ratio of 0.69 (LTG vs. OTG, 95% confidence interval, 0.52 to 0.91). Moreover, the hazard ratio of Siewert type II was 0.79 (95% confidence interval, 0.46 to 1.12) and that of Siewert type III was 1.16 (95% confidence interval, 0.78 to 1.54).

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Conclusion: It can thus be seen that LTG is a safe and effective method for treating patients with advanced Siewert type II and type III AEG and patients with Siewert type II AEG may benefit more from LTG in the long term.
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1. Introduction

Currently, there is a higher diagnosis rate for adenocarcinoma of the esophagogastric junction (AEG), classified as Siewert type I, type II, and type III.[1] Hence, a relatively high proportion of gastric cancer surgery includes total gastrectomy of Siewert type II and type III. With doctors as well as patients recognising the advantages of minimally invasive laparoscopic surgery, this surgery becomes more popular for patients with gastric cancer.[2] Although the application of laparoscopic total gastrectomy (LTG) in advanced tumour stage remains controversial, several hospitals with extensive experience in laparoscopic surgery for gastric cancer have already conducted LTG in clinical practise. Therefore, it is necessary to obtain the supporting evidence for applying LTG in advanced gastric cancer. The present study performed a retrospective data analysis of total gastrectomy for advanced Siewert type II and type III AEG in a single centre and aimed to compare the short-term and long-term outcomes of LTG and traditional open total gastrectomy (OTG) as well as discuss the feasibility of LTG for advanced Siewert type II and type III AEG in clinical practise.

2. Methods

2.1. Patients enrolment

From January 2012 to December 2017, there were 872 patients with advanced Siewert type II and type III AEG who were going to be treated with total gastrectomy in our department. All 872 patients' data were screened, and 32 patients with gastric stump cancer and 60 patients who had been treated with combined organs resection were excluded from this study. Additionally, 58 patients were examined only using laparoscopic exploration, and laparoscopic biopsy and palliative surgery (such as bypass and jejunum stoma) were ruled out. Finally, 722 patients were enrolled for this study who were then divided into two groups, LTG and OTG, according to the surgical approach that they had received. It was not possible, however, to compare the patients in these two groups as they had different clinical baselines and diseases. To eliminate this bias, propensity score match (PSM) was used to counter the difference between these two groups. Out of the 722 patients, 685 were propensity score matched, of which 468 patients were treated with LTG, and 217 patients underwent OTG (Fig. 1).

2.2. Statistical analysis

Though the definition of advanced gastric cancer is still debated, it is generally accepted that advanced gastric cancer is recognized by T stage which represents the depth of the tumour's invasion. $T \geq 2$ (tumour reaches the muscle layer of the stomach or deeper) with any N stage is classified as advanced gastric cancer.[3] The Siewert type classification was conducted before surgery according to the gastroscope or endoscopic ultrasonography (EUS) and computed tomography (CT), with or without upper gastrointestinal contrast, results. The American Society of Anaesthesiologists definition was used to score ASA. Moreover, the comorbidities in this study were classified as diabetes, hypertension, ischemic heart disease, and steroid usage, while comorbidities apart from these were all categorised as 'others' (such as Alzheimer's disease and chronic obstructive pulmonary disease). Further, the postoperative complications were classified as bleeding, anastomotic leakage, ileus, pneumonia, surgical site infection (SSI), and pancreatic fistula, while other complications were categorised as 'others' (such as heart attack, pulmonary embolism, and cerebral ischemic stroke). Pain scores were recorded using the Visual Analogue Scale (VAS) (0 = no pain, 10 = worst pain).

The primary endpoint was the overall survival (OS) which is defined as the duration between surgery and death caused by any reason. Secondary endpoints included disease-free survival (DFS), which is defined as the duration between surgery and first recurrence or death caused by any reason. This can include the number of harvested lymph nodes, postoperative CRP level, pain score, length of postoperative stay, time required for tolerating liquid food, time required for ambulation, time required for restoring bowel function, and postoperative complications with severity graded as per the Clavien-Dindo classification.[4]

A calliper width of 0.05 of the standard deviation of the propensity score logistic was also imposed. Patients were matched according to the nearest neighbour with matching principle under the allocation numbers 2:1. The Chi-squared or Fisher's exact test was used to evaluate categorical variables while the unpaired Student's t-test or the Mann Whitney U test was used for analysing continuous variables. Moreover, the Kaplan—Meier method was used for assessing the OS and DFS for the two groups, and the groups were then compared using the log-rank test. The multiple Cox regression model was applied for estimating the HR and 95% confidence intervals (CI). All statistical tests were two-sided, with P values of 0.05 or less being considered statistically significant. Statistical analyses were performed using GraphPad Prism 7.0 (GraphPad

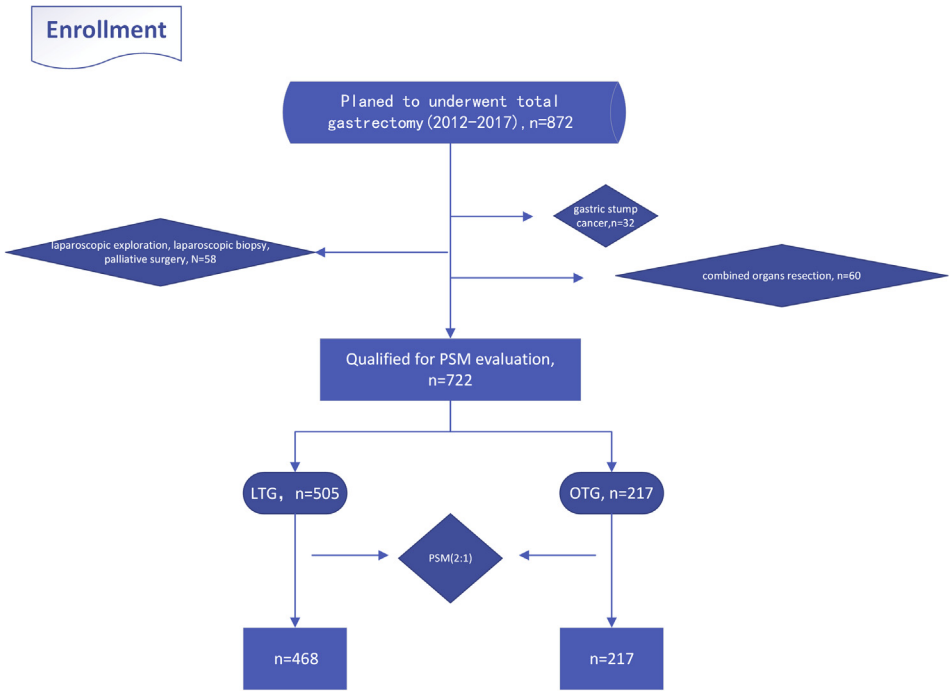

Figure 1 The flowchart of patient enrolment.

Software Inc., La Jolla, CA), Stata 14 (StataCorp, College Station, TX), and MedCalc 15.8 (MedCalc Software BVPA, Ostend, Belgium).

3. Results

3.1. Patients characteristics

There were different baselines for all the patients ($n = 722$) in LTG and OTG groups before they were propensity score-matched ($p < 0.05$). To ensure that these two groups could be compared, the patients' age, gender, body mass index (BMI), ASA score, tumour size, Siewert type, clinical T stage, clinical N stage, comorbidities, and whether they had been treated with neoadjuvant chemotherapy were established as variables. These variables were used to conduct a PSM analysis, and all variables applied in PSM were preoperative indicators. This is how these two groups were brought to the same baseline, and there were no longer significant differences in the two groups' clinical preoperative characteristics ($p > 0.05$). The summary of the enrolled patients' clinical characteristics is shown in Table 1, and the matching results are illustrated in Fig. 2.

3.2. Surgery finding and short-term outcomes

Between these two propensity score-matched groups, differences were noted in the operation time (LTG vs. OTG, 68.04 ± 9.65 min vs. 80.17 ± 7.81 min, $p < 0.001$) and the amount of blood loss during operations (LTG vs. OTG, 98.64 ± 29.99 ml vs. 220.8 ± 53.34 ml, $p < 0.001$). There also were no differences in the reconstruction methods ($p < 0.01$).

During the first two postoperative days, the patients' C reactive protein (CRP) level was observed. The nurses collected their blood samples at 6:00 am. On the first postoperative day (POD 1), the LTG group showed lower CRP level (30.1 ± 6.20 mg/L) compared to OTG group (40 ± 6.26 mg/L) ($p < 0.001$), and similar results regarding the about CRP level were observed on the second postoperative day (POD2) (LTG vs. OTG, 68.04 ± 9.65 mg/L vs. 80.17 ± 7.81 mg/L, $p < 0.001$). The nurses also assessed the pain score and observed that the patients in the LTG group scored 4.57 ± 1.11 on POD1 while patients of OTG group scored 5.49 ± 1.91 ($p < 0.001$). On POD2, compared to the OTG group, LTG groups seemed to continue experiencing less pain (LTG vs OTG, 3.54 ± 1.19 vs 5.52 ± 1.19, $p < 0.001$).

Patients in the LTG group were able to tolerate liquid food 1.53 ± 0.50 days after the operation, while patients in the OTG group needed 2.90 ± 0.83 days ($p < 0.001$). The length of postoperative stay for the two groups also differed (LTG vs OTG, 7.46 ± 1.11 days vs 9.49 ± 1.08 days, $p < 0.001$). Further, patients in the LTG group were able to restore intestinal function more rapidly (LTG vs. OTG, 1.95 ± 0.83 vs. 3.97 ± 0.80 postoperative days, $p < 0.001$) and were able to walk after 1.99 ± 0.82 postoperative days, which is fewer days than the patients in the OTG group required (3.77 ± 0.72 days, $p < 0.001$). No significant difference was observed in the two groups in the pTNM stage ($p = 0.16$) and in the number of lymph nodes harvested (LTG vs OTG, 36.1 ± 7.67 vs 35.25 ± 7.78, $p = 0.18$).

No differences were seen in the two groups' complication rate ($p = 0.19$) as well as concerning the severity of postoperative complications ($p = 0.7$). Although 30 days after the surgery, three patients were readmitted, two patients died from the LTG group while two patients were

Table 1 Basic characteristics before and after PSM.

Characteristics	All patients (n = 722)					Propensity-matched patients (n = 685)				
	LTG (n = 505)	%	OTG (n = 217)	%	P value	LTG (n = 468)	%	OTG (n = 217)	%	P value
Age(mean ± SD)	60.16 ± 10.61		62.45 ± 10.58		0.008	60.42 ± 10.40		58.99 ± 10.58		0.07
Gender					0.003					0.18
Male	354	70.10	175	80.65		330	70.51	175	80.65	
Female	151	29.9	42	19.35		138	29.49	42	19.35	
BMI (kg/cm^2) (mean ± SD)	22.39 ± 2.63		23.21 ± 2.61		0.000	22.51 ± 2.61		22.71 ± 2.61		0.22
ASA					0.024					0.76
1	43	8.51	22	10.14		40	8.55	22	10.14	
2	137	27.13	26	11.98		121	25.85	26	11.98	
3	325	64.36	169	77.88		307	65.6	169	77.88	
Tumor size					0.000					0.73
<5 cm	332	65.74	109	50.23		300	64.1	109	50.23	
≥5 cm	173	34.26	108	49.77		168	25.9	108	49.77	
Siewert type					0.000					0.20
TypeII	177	35.05	45	20.74		150	32.05	45	20.74	
Type III	328	64.95	172	79.26		318	67.95	172	79.26	
Clinical T stage					0.002					0.35
T2	44	8.71	7	3.23		37	7.9	7	3.23	
T3	323	63.96	132	60.83		301	64.32	132	60.83	
T4a	133	26.34	75	34.56		125	26.71	75	34.56	
T4b	5	0.99	3	1.38		5	1.07	3	1.38	
Clinical N stage					0.000					0.06
N0	113	22.38	17	7.83		86	18.38	17	7.83	
N1～3	392	77.62	200	92.17		382	81.62	200	92.17	
Comorbidities					0.029					0.12
Diabetes	29	5.74	16	7.37		28	5.98	16	7.37	
Hypertension	48	9.5	24	11.06		46	9.83	24	11.06	
Ischemic heart disease	31	6.14	19	8.76		31	6.62	19	8.76	
Steroid usage	18	3.56	12	5.53		18	3.85	12	5.53	
Others	30	5.94	16	7.37		29	6.2	16	7.37	
Neoadjuvant chemotherapy					0.000					0.08
Yes	94	18.61	9	4.15		61	13.03	9	4.15	
No	411	81.39	208	95.85		407	86.96	208	95.85	

readmitted and one patient died from the OTG group, no significant differences were observed. Further details regarding surgery's findings and short-term outcomes are showed in Table 2.

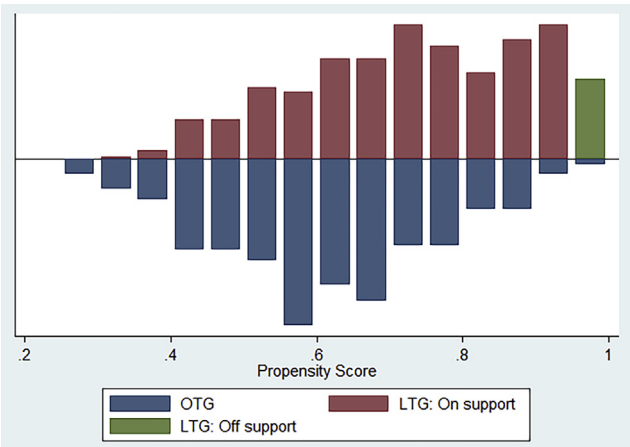

Figure 2 The results of propensity score match.

3.3. Long-term outcomes

For the LTG and OTG groups, the median survival time was 56 months and 47 months, respectively, and the 5-year overall survival probability was 40% and 29.1%, respectively. Compared to the OTG group, the LTG group had better overall survival (OS) rate ($p < 0.01$), with the hazard ratio (LTG vs OTG) for OS being 0.69 (95% CI, 0.52 to 0.91) (Fig. 3). Similarly, the LTG group had better disease-free survival (DFS) than the OTG group ($p < 0.001$), with the hazard ratio (LTG vs OTG) for DFS being 0.65 (95% CI, 0.51 to 0.83). The median disease-free survival time was 50 months and 41 months for the LTG group and OTG group, respectively (Fig. 4). Furthermore, considering all variables, a multiple Cox regression model indicated that the surgical approach was an independent risk factor for OS,

Table 2 operating findings and postoperative outcomes.

	LTG (n = 468)	%	OTG (n = 217)	%	P value
Operating time, min	155.2 ± 25.46		143.4 ± 18.55		<0.001
Blood loss, ml	98.64 ± 29.99		220.8 ± 53.34		<0.001
Reconstruction					<0.01
Roux-en-Y	426	91.03	183	84.33	
Others	42	8.97	34	15.67	
CRP POD1 mg/L	30.1 ± 6.20		40 ± 6.26		<0.001
CRP POD2 mg/L	68.04 ± 9.65		80.17 ± 7.81		<0.001
Pain score POD1	4.57 ±1.11		5.49 ± 1.91		<0.001
Pain score POD2	3.54 ± 1.19		5.52 ± 1.19		<0.001
Pathologic T stage					0.17
T2	37	7.91	15	6.91	
T3	301	64.32	132	60.83	
T4a	104	22.22	50	23.04	
T4b	26	5.55	20	9.22	
Pathologic N stage					0.38
N0	86	18.38	27	12.44	
N1	265	56.62	138	63.6	
N2	91	19.44	40	18.43	
N3	26	5.56	12	5.53	
pTNM					0.16
IB	7	1.5	2	0.92	
IIA	86	18.38	28	12.9	
IIB	182	38.89	94	43.32	
IIIA	122	26.07	52	23.96	
IIIB	60	12.82	33	15.21	
IIIC	11	2.34	8	3.69	
LN harvested	36.1 ± 7.67		35.25 ± 7.78		0.18
Postoperative hospital stay (days)	7.46 ± 1.11		9.49 ± 1.08		<0.001
Time to take liquid food (days)	1.53 ± 0.50		2.90 ± 0.83		<0.001
Time to first flatus or defecation (days)	1.95 ± 0.83		3.97 ± 0.80		<0.001
Time to ambulation (days)	1.99 ± 0.82		3.77 ± 0.72		<0.001
Complications					0.19
Bleed	8	1.71	4	1.84	
Anastomotic leakage	21	4.49	8	3.69	
Ileus	14	2.99	8	3.69	
Pneumonia	10	2.14	8	3.69	
SSI	17	3.63	11	5.07	
Pancreatic fistula	11	2.35	6	2.76	
Others	4	0.85	3	1.38	
Grade of complications					0.70
Grade 2	53	11.32	27	12.44	
Grade 3	25	5.34	17	7.83	
Grade ≥4	7	1.5	4	1.84	
Readmission in 30 days	3	0.64	2	0.92	0.68
Mortality in 30 days	2	0.43	1	0.46	0.95

with the hazard ratio (LTG vs OTG) being 0.59 (95% CI, 0.42 to 0.83) (Fig. 5).

4. Discussion

PSM is a statistical matching technique that accounts for the covariates that predict the receiving of the treatment to estimates a treatment's effect. PSM attempts to reduce the bias caused by confounding variables that may occur in an estimate of the treatment's effect. There has been widespread use of PSM in medical research of late.[5] This is primarily because of its undeniable convenience. Randomized controlled trial (RCT), on the other hand, is time-consuming as well as expensive. Conducting RCTs requires a significant amount of work. Hence, in the real world study, PSM is a useful and powerful instrument for evaluating medical data. It should be noted, however, that some studies have incorrectly calculated PSM. For example, several postoperative parameters have been included for PSM that may lead to biased conclusions. To ensure the validity of the present study's findings, the variables used in

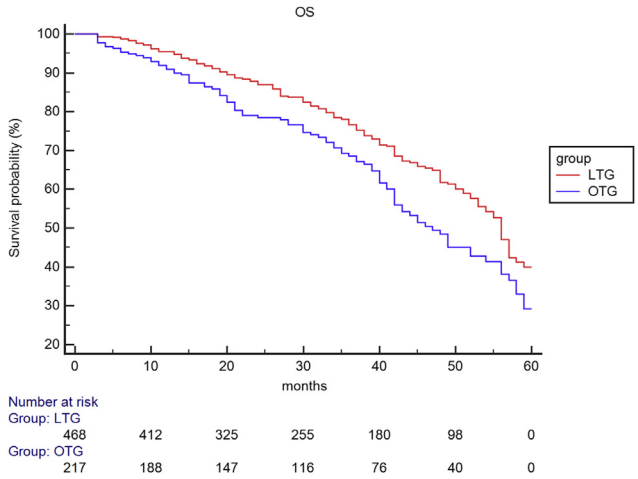

Figure 3 5-year OS (LTG/OTG, HR = 0.69, 95% CI 0.52—0.91).

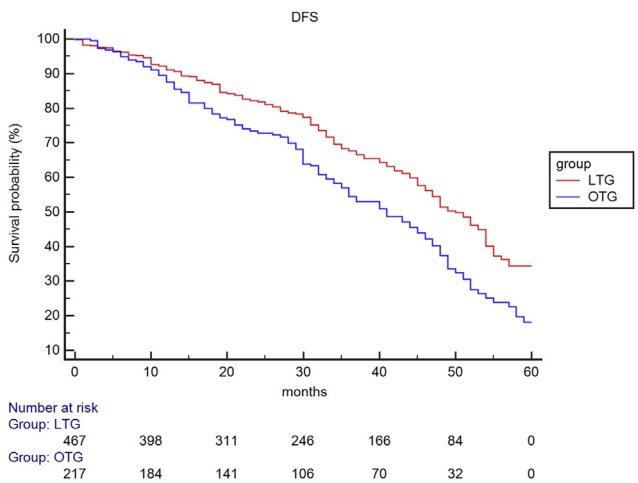

Figure 4 DFS (LTG/OTG, HR = 0.65, 95% CI 0.51—0.83).

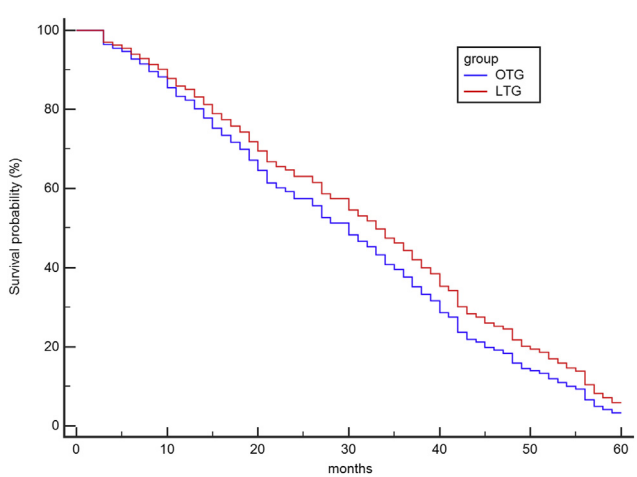

Figure 5 Survival curve grouped by surgical approach. HR 0.59 (95% CI, 0.42 to 0.83).

PSM were selected strictly. This also helped in limiting the doctors' judgement bias. That is, doctors were not able to make biased decisions regarding their surgical approach based on the patients' preoperative data.

Recently, prospective clinical trials such as JCOG-0703[6] in Japan and KLASS-01[7] in South Korea have demonstrated the safety of laparoscopy-assisted distal gastrectomy (LADG). These trials, however, only focused on particular patient groups that had stage I gastric cancer. For advanced gastric cancer (T2-4aN0 ~ 3M0), the CLASS-01 study in China only accomplished enrolment. According to preliminary findings, in cases of advanced distal gastric cancer, it is safe to conduct laparoscopic radical gastrectomy.[8] Both JCOG-1401 study in Japan and CLASS -02 research in China are continuing their work for assessing the safety as well as the feasibility of LTG and laparoscopy-assisted proximal gastrectomy (LAPG) to treat early gastric cancer. The CLASS -02 research is a multicentre randomized controlled clinical trial that compares the safety of laparoscopic and open radical gastrectomy and is being conducted by Professor Yihong Sun, Zhongshan Hospital of Fudan University. The fact, however, that most patients in China are diagnosed at a relatively late stage cannot be ignored. LTG has, in fact, already been applied in clinical practise even without reliable evidence that proves its feasibility. To fill these evidence gaps while awaiting the outcomes of clinical trials, similar to several other investigators, our database was used to conduct this analytical study. According to the results, it can be seen that LTG can be safely and effectively used in clinical practise.

As depicted in Table 2, although patients in the LTG group experienced longer operation time, they had less blood loss during operations than those in OTG group. This is understandable because the process of meticulous dissection through instruments and screens is indeed time-consuming. Blood loss can be reduced by careful identification using laparoscope. Regarding the reconstruction method, several types of styles have been attempted in LTG, such as Un-cut Roux-en-Y[9] and Overlap.[10] This method has also been applied to open surgery. Considering the occurrence of anastomotic stenosis, it is clear that none of these are suitable.[11] In this study, the reconstruction method was classified into two categories: Roux-en-Y and others. This may be the reason for them being statistically different.

Siewert type is classified as follows: type I where the centre of AEG is located 1—5 cm above the esophagogastric junction (EGJ); type II where the centre of AEG is located 1 cm above to 2 cm below the EGJ; and type III where the centre of AEG is located 2—5 cm below the EGJ.[12] All surgical approaches for Siewert type II and type III gastric cancer were standard D2 resection, both of which were in LTG and OTG groups. There were no differences in the pT stage, pN stage, and pTNM stage as well as in the number of harvested lymph nodes. Thus, concerning all Siewert type II and type III gastric cancer stages, LTG and OTG are equally capable of making radical resection that meets the D2 criterion.

Surgical stress can affect a series of physiological processes in patients' bodies, such as neuroendocrine, haemodynamics, metabolism, and immunity. The level of stress, in turn, can directly impact patients' postoperative

recovery.[13] The level of CRP, which is an acute reactive protein produced by the liver, can be significantly increased under stress, thus reflecting the intensity of stress.[14] Another indicator of stress is pain.[15] There was an increase in the CRP level for both LTG and OTG groups during the first two postoperative days. The OTG group, however, had a higher CRP level during these two days compared to the LTG group (Fig. 6A). Further, during the first two postoperative days, patients in the LTG group experienced less pain than those in the OTG group, and the LTG group's pain score decreased on POD2, while there were no notable changes for the OTG group (Fig. 6B).

The results of these two indicators clearly showed that LTG caused less stress on patients than OTG, which justified the relatively fast recovery of the LTG group. Patients in the LTG group took less time to tolerate liquid food, to walk, and to restore bowel function. They thus had a shorter postoperative stay than those in the OTG group. These data properly embodied the effectiveness of LTG (Fig. 6C).

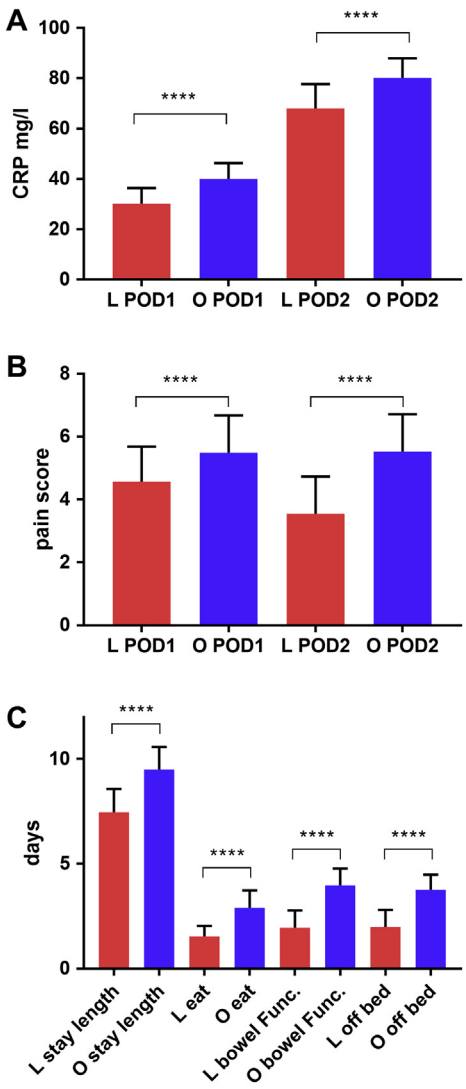

Figure 6 Comparison of short-term outcomes between LTG and OTG group. 6-A: CRP level in LTG and OTG group. 6-B: pain score comparison. 6-C: Comparison of recovery indicators. L: LTG group. O: OTG group. POD1: postoperative day 1. POD2: postoperative day 2. stay length: days patients stay in hospital after surgery. eat: days patients took to be able to take liquid food orally after surgery. bowel Func.: days patients took to restore intestinal function after surgery (defecation or flatus). off bed: days patients took to get off bed to walk.

Several researchers have already recognised the efficiency of the Clavien-Dindo classification system. In the present study, the postoperative complication rates of LTG and OTG groups were 18.1% and 22.1%, respectively. According to the data was collected from 2012 to 2017, the development of the laparoscopic technique in our department should not be ignored. The technique was gradually improved, and currently, the complication rates of LTG and OTG in our department are significantly lower than those stated previously. This is despite the fact that there was no difference in both the occurrence ($p = 0.19$) and severity grade ($p = 0.7$) of postoperative complication. There was also no statistical disparity in the readmission rate and mortality during the 30 days after surgery. Overall, the safety of LTG was well presented.

As shown in Fig. 3, the LTG group had better OS than the OTG group. The 5-year overall survival probability for the LTG and OTG groups was 40% and 29.1%, respectively. These are considerably lower than that stated in other scholars' report. For example, Takahiro Kinoshita's study[16] showed that there was 54.2% and 53% 5-year OS probability for laparoscopic gastric surgery and open gastric surgery, respectively. Ki-Han Kim[17] reported 70.8% 5-year OS probability. It should, of course, be noted that there were different conditions and different data for each study. The abovementioned study either considered other surgical approaches besides total gastrectomy or confined the study objects to young patients. Regardless, the results of the present study portray the current situation about surgery regarding the advanced Siewert type II and type III AEG in our department. Patients in both groups mostly carried tumours with pathological stage through IIB to IIIB, which can account for the low 5-year OS probability.

To determine Siewert type's role in patients' OS, as well as for other variables in this study, the Cox proportional hazards model for OS was applied. The results are presented in Fig. 7.

It was observed that HR of Siewert type II was 0.79 (95% CI, 0.46—1.12) which gave a better prognosis for patients who were classified as Siewert type II AEG and treated by LTG. That is, Siewert type II AEG can be better treated by laparoscopy. Siewert type II AEG is located 1 cm above to 2 cm below the EGJ, which is neither too high nor too low. The surgical vision field is quite limited if OTG is chosen for Siewert type II AEG. It is sometimes impossible to dissect lymph nodes around lower oesophagus because surgeons are unable to see them in OTG. Laparoscope can help resolve this problem as it can help surgeons have better surgical vision and can help in proper dissection in locations that surgeons' hands cannot reach. The advantages of laparoscope also make the surgeons' more enthusiastic about conducting LTG for Siewert type II AEG as well as type III as it ensures a safe and effective approach when dealing with AEG. The present study's data also demonstrated the advantages of LTG. Theoretically, though the advantages are also valid for Siewert type III AEG, the results showed

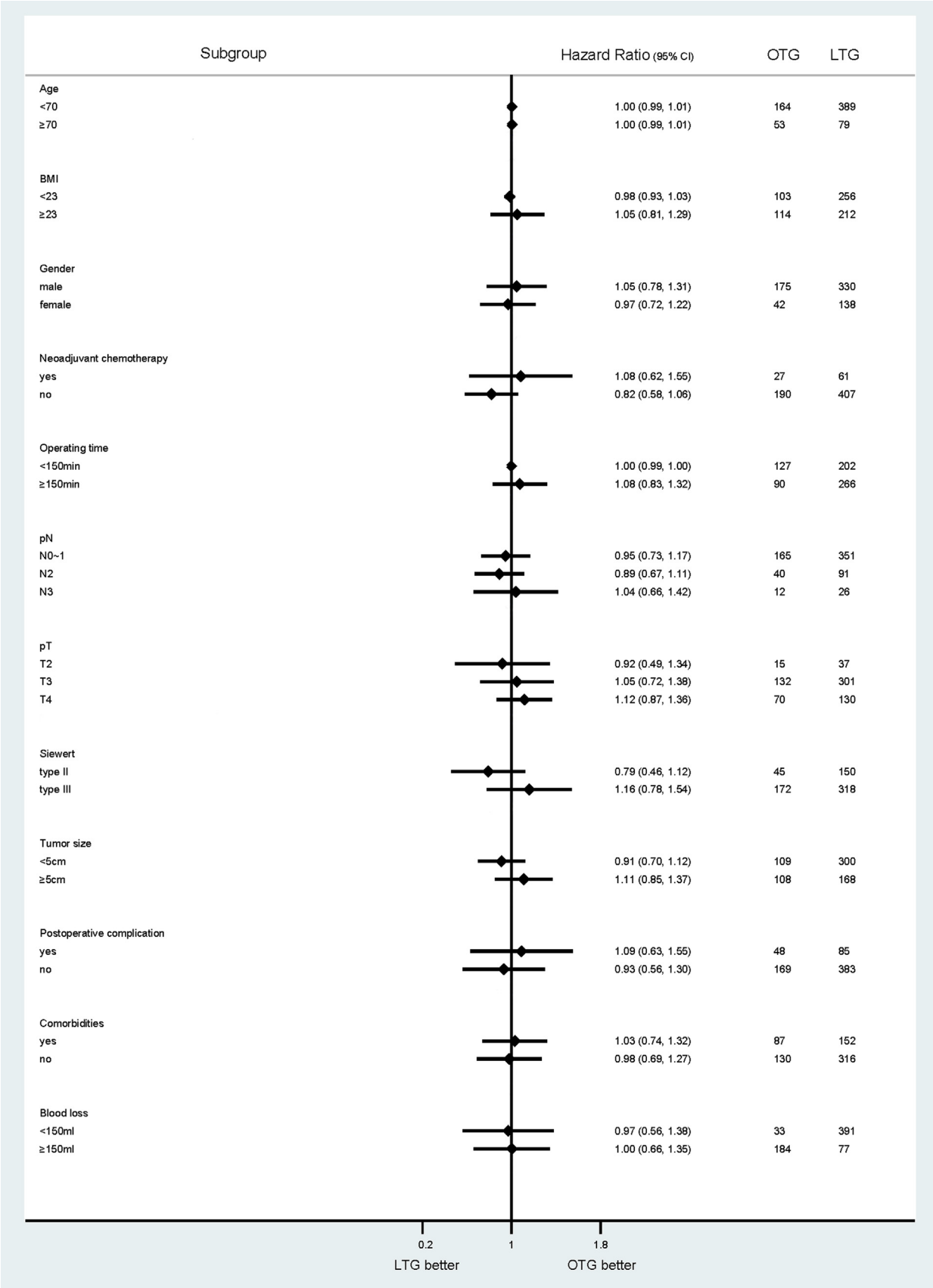

Figure 7 Forest Plot of HR for OS (LTG vs. OTG).

that patients with Siewert type III AEG were unable to benefit from LTG. It is possible that the advantages of laparoscope were compensated by the surgeons' surgical techniques as relatively lower dissection height is needed around lower oesophagus when dealing with Siewert type III AEG. Another reason may be that further improvements to the LTG techniques are needed.

As depicted in the HR forest plot, whether to receive neoadjuvant chemotherapy has different HR for OS. That is, patients treated by LTG having no preoperative neoadjuvant chemotherapy can gain better OS. When no neoadjuvant chemotherapy is needed, it indicates that the tumour is in a relatively early disease stage. The effect of pTNM on OS needs no further discussion. Thus, it is possible to predict the neoadjuvant chemotherapy results.

The HR forest plot also helps audiences to build a conception of LTG admittance criterion As LTG is not suitable for every patient.

This study undoubtedly has some limitations. First, it was a retrospective analysis despite carefully designing PSM for underlying factors. Hence, this study's findings have limited reliability. Large-scale and elaborately designed random trials are required for verifying this study's results. Second, the surgical strategies for treating Siewert type II AEG remain controversial.[18] In this study, total gastrectomy was performed for Siewert type II AEG. It should, however, be noted that esophagectomy can also be performed for type II AEG.[19] Thus, it remains to be determined which of these two surgeries is better. Third, the neoadjuvant chemotherapy admittance criterion is not universal, with regimens differing according to different doctors and departments. Furthermore, the effectiveness of neoadjuvant chemotherapy remains inconclusive.[20,21] This factor was not taken into consideration in this study. Finally, this study also failed to consider the development of surgeons' surgical technique, which may, to an extent, affect the outcomes. Despite these limitations, the application of LTG in advanced Siewert type II and type III AEG is important.

Therefore, this study's findings firmly suggested that LTG is a safe and effective method for treating patients with advanced Siewert type II and type III AEG and that patients with Siewert type II AEG may benefit more in the long term from LTG. The validity of these results, however, should be verified through random trials on a large scale.

Conflicts of interest

No conflicts of interest need to be declared.

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