



Clinical outcomes of proximal gastrectomy versus total gastrectomy for locally advanced proximal gastric cancer: a propensity score matching analysis

Lulu Zhao^{1#}, Rui Ling^{2#}, Fuhai Ma¹, Hu Ren¹, Hong Zhou¹, Tongbo Wang¹, Yingtai Chen¹, Shangying Hu¹, Dongbing Zhao¹

¹National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China; ²Department of Microbiology and Immunology, Georgetown University Medical Center, Washington, DC, USA

Contributions: (I) Conception and design: Y Chen, L Zhao; (II) Administrative support: D Zhao; (III) Provision of study materials or patients: F Ma, H Ren; (IV) Collection and assembly of data: R Ling, H Zhou, T Wang; (V) Data analysis and interpretation: S Hu, L Zhao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yingtai Chen, MD, PhD; Shangying Hu, PhD; Dongbing Zhao, MD, PhD. National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 17 Panjiayuan Nanli, Beijing 100021, China. Email: yingtaichen@126.com; shangyinghu@cicams.ac.cn; dbzhao2003@sina.com.

Background: The safety and efficacy of proximal gastrectomy (PG) following for locally advanced proximal gastric cancer (LAPGC) were unclear, as oncologic outcomes of randomized trials are still pending. The aim of this study was to evaluate surgical results and long-term oncologic outcomes of PG versus total gastrectomy (TG) in treating locally advanced gastric cancer (LAGC).

Methods: A total of 2,918 LAPGC patients with PG or TG were identified from the China National Cancer Center Gastric Cancer Database (NCCGCDB) 1998–2018. Propensity score matching was employed to match patients with PG or TG in a 1:1 ratio. Surgery outcomes and overall survival (OS) rates were compared between PG and TG groups after the propensity-score match. Cox proportional hazards model was used to explore the risk factors for OS.

Results: Of 2,918 patients, 181 (6.20%) underwent TG, while 2,737 (93.80%) underwent PG. After propensity score matching, 150 matched pairs for PG and TG were selected. Compared with TG group, PG group had shorter operative time (181.8±49.8 *vs.* 213.5±66.7 min, *P*<0.001) and less estimated blood transfusion (10.00% *vs.* 22.67%, *P*=0.001). More lymph nodes (34.3±17.0 *vs.* 24.2±11.0, *P*<0.001) were retrieved in TG group than in PG group. The 3- and 5-year OS rates (79.1% *vs.* 77.2% and 74.5% *vs.* 72.0%, respectively, both *P*<0.001) in PG group were slightly higher than ones in TG group. However, the multivariable results showed that there was no significant difference in the OS status between the two groups (HR: 1.172, 95% CI: 0.916–1.499, *P*=0.208), even stratified into stage II and III subgroup.

Conclusions: In conclusion, the extent of resection for LAPGC patients did not influence the long-term survival outcomes. Moreover, future randomized clinical trials of quality of life following PG or TG are expected to assist surgeons in the choice of surgical approach and strategy for LAPGC patients.

Keywords: Locally advanced proximal gastric cancer (LAPGC); proximal gastrectomy (PG); total gastrectomy (TG); survival

Submitted Nov 19, 2019. Accepted for publication Feb 03, 2020.

doi: 10.21037/tcr.2020.02.38

View this article at: <http://dx.doi.org/10.21037/tcr.2020.02.38>

Introduction

Gastric cancer remains a worldwide cancer with the third most frequent cause of cancer-related deaths (1). Although the overall incidence of gastric cancer has been declining in Western and Eastern countries, the incidence of carcinoma of the upper-third of the stomach has been increasing at an alarming rate (2-4). Furthermore, cancer-related mortality of proximal is higher than other sites of stomach (5). Given these characteristics of proximal gastric cancer (PGC), the optimal surgical selection has received considerable attention.

For early PGC, proximal gastrectomy (PG) has been generally accepted by most surgeons for its oncological radicality and safety (6-15). However, concerning to locally advanced PGC (LAPGC), it still has not reached a consensus. Proponents (10,16,17) of PG have argued that PG can achieve an equivalent overall survival (OS) compared to total gastrectomy (TG), whereas others (18,19) showed that TG was associated with better 5-year OS. Moreover, there was no clinical outcome of clinical randomized trial targeting the same issue.

Given the suggested but undecided survival differences between PG and TG, the aim of our study was to compare the clinicopathologic features, surgical and survival outcomes for LAPGC patients with either PG or with TG based on the China National Cancer Center Gastric Cancer Database (NCCGCDB), in order to provide evidences for the development of guiding strategies for LAPGC patients.

Methods

Patient population

All the study data were abstracted from the NCCGCDB. The NCCGCDB was a clinical gastric cancer database based on a huge retrospective cohort, which was sourced from China National Cancer Center, a single but large-volume institution, and included more than 19,000 patients from all around China 1998 to 2018. LAPGC was defined as clinical stage IB–III (according to the eighth edition of the International Union against Cancer Classification) with the epicenter located in cardia (C16.0) or fundus (C16.1). The extent of gastric resection, TG or PG, was dictated by tumor size and epicenter, tumor stage, the potential volume of the future remnant stomach, and surgeon's preference. Finally, 2,737 PG patients and 181 TG patients were identified during 1998 to 2018 year. This study was approved by the ethics committee of National Cancer

Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 17-156/1412), and informed consent was taken from all patients.

Statistical analyses

Patient demographics and clinical characteristics between PG and TG groups were compared with *t*-test for continuous variables with normal distribution and chi-square test for categorical variables.

Given the inherent differences between patients in PG and TG groups, we calculated a propensity score for following variables: gender, age, smoking, drinking, HER2 score, *H. pylori* infection, Lauren classification, histologic type, linitis plastica, nerve invasion, vascular invasion, pTNM, adjuvant therapies, BMI and no. of lymph nodes metastasis. The propensity score was estimated using a logit model. Matching was performed using a 1:1 optimal matching method with 0.2 of caliper value, which yielded 150 pairs of TG and PG patients. Surgical and OS outcomes after surgery were compared within the propensity-score matched cohorts. Three- and five-year OS rates were calculated with the Kaplan-Meier method and compared by Z test. The differences of OS during the whole follow-up period between two groups were assessed using the log-rank test when two survival curves didn't cross otherwise using two-stage hazard rate comparison method (20). To find risk predictors of all-cause mortality in the matched population, the following variables were evaluated in a univariate model: gender, age, smoking, drinking, HER2 score, *H. pylori* infection, Lauren classification, histologic type, linitis plastica, nerve invasion, vascular invasion, pTNM stage, surgical margin, adjuvant therapies. Then, hazard ratio (HR) and 95% confidence interval (CI) were calculated by a multivariate analysis using the Cox proportional hazard regression model.

A P value less than 0.05 was considered statistically significant and all tests were two-sided. Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and Rstudio (RStudio, Inc., Boston, MA, USA).

Results

Clinicopathologic characteristics

In this study, 2,918 patients were included. The clinicopathologic features of 181 patients (6.20%) with

TG and 2,737 patients (93.80%) with PG were compared (Table 1). Clearly, a higher PG proportion was found in the LAPGC in China National Cancer Center. The median follow-up times were 62.7±3.5 months in PG group and 45.9±5.6 months in TG groups.

Compared to TG groups, patients in the PG group were more likely to be older age (≥65 years, 40.23% vs. 32.59%, $P=0.04$), smoking history (55.72% vs. 41.99%, $P=0.002$), and intestinal type (28.06% vs. 18.78%, $P<0.001$). Patients in TG group were also more likely to have more HER2 negative (42.54% vs. 23.20%, $P<0.001$), nerve invasion (51.93% vs. 33.39%, $P<0.001$), vascular invasion (45.86% vs. 34.64%, $P=0.006$), and to be in later pN stage (N2 and N3, 48.61% vs. 38.92%, $P=0.04$). In addition, the metastasis rate of the total number of resected lymph nodes was significantly higher in the TG group compared to PG group ($P=0.02$).

After propensity score matching, 150 matched pairs for PG vs. TG were selected. Patients who underwent PG were also more likely to be in earlier pT stage (pT4, 22.67% vs. 36.00%, $P=0.02$) comparing with TG group. As for other clinicopathologic characteristics, there was no significant difference between the two groups ($P>0.05$) (Table 1).

Surgical outcomes after propensity score matching

The surgical outcomes after propensity score matching of LAPGC patients undergoing PG and TG were detailed in Table 2. No significant differences between the two groups in negative surgical margin (92.67% vs. 97.33%, $P=0.158$), postoperative mortality (0.67% vs. 0.67%, $P=1.00$) and postoperative stay (12 vs. 11 days, $P=0.64$). A higher proportion of open gastrectomy (97.33% vs. 69.33%, $P<0.001$) and a lower proportion of laparoscopy-assisted gastrectomy (1.33% vs. 26.00%, $P<0.001$) was showed in PG patients than TG group. When compared with TG group, PG group was associated with shorter operative time (181.8±49.8 vs. 213.5±66.7 min, $P<0.001$). The mean estimated blood transfusion of the PG group was 235 mL less than that of TG group (743.8±296.6 vs. 978.4±421.1 mL, $P=0.049$). However, the no. of retrieved lymph nodes (34.3±17.0 vs. 24.2±11.0, $P<0.001$) in TG group was larger than PG.

Survival outcomes after propensity score matching

Kaplan-Meier survival curves of LAPGC patients following PG and TG were showed in Table 3 and Figure 1A.

Although the OS rates following PG and TG had no statistically significant differences during the long-term follow-up period ($P=0.62$), the 3- and 5-year OS rates (79.1% vs. 77.2% and 74.5% vs. 72.0%, respectively, both $P<0.001$) in PG group were slightly higher than ones in TG group. Concerning to detailed group for stage, PG patients of stage II only had a higher 5-year OS rate (85.7% vs. 81.7%, $P<0.001$) while ones of stage III showed both improved 3- and 5-year OS rates (73.3% vs. 65.2% and 68.8% vs. 62.4%, respectively, both $P<0.001$) (Figure 1B,C, Table 3). After controlling for confounding variables (Table 4), the multivariable results from Cox proportional hazards regression analysis also showed that the extent of resection had no impact on the long-term OS status (HR: 1.172, 95% CI: 0.916–1.499, $P=0.208$), even stratified into stage II and III (Tables S1,S2).

Prognostic factors of survival in univariate and multivariate analyses

As shown in Table 4, univariate analyses of LAPGC patients revealed significantly different survival based on the following parameters: gender, HER2 positive (+++), diffuse type, linitis plastica, and pTNM stage. When appropriate significant factors were taken into consideration, multivariate analysis revealed HER2 positive (+++), *H. pylori* infection, linitis plastica and pTNM stage were independent predictors for poor prognosis.

Discussion

To date, we found that only two large-scale randomized trials (Trial registration number: NCT01433861 and NCT02892643) targeting the same issue are currently underway, and surgeons are awaiting the results. Realistically, many surgeons are now actively applying PG to LAPGC. To our best knowledge, our analysis represented the largest evaluations of outcomes for LAPGC patients undergoing PG or TG. A major finding of our study was that PG was an optional surgical procedure of LAPGC treatment for its better 3-, 5-year survival rates when compared to TG.

In this large retrospective cohort study from the NCCGCDB, the number of patients varies significantly between the two groups, with an incidence of TG: PG = 1: 16. There were some possible reasons for this quantitative difference. Firstly, more and more studies have proved that TG was not always necessary for LAPGC (10,16,17,21-23).

Table 1 Comparison of patient characteristics

Characteristics	Overall (N=2,918)			Propensity score matched (N=300) ¹		
	TG group (N=181)	PG group (N=2,737)	P value	TG group (N=150)	PG group (N=150)	P value
Gender, n (%)			0.67			1.00
Male	150 (82.87)	2,301 (84.07)		127 (84.67)	127 (84.67)	
Female	31 (17.13)	436 (15.93)		23 (15.33)	23 (15.33)	
Age, n (%)			0.04			1.00
<50	26 (14.36)	276 (10.08)		21 (14.00)	21 (14.00)	
50–64	96 (53.04)	1,360 (49.69)		82 (54.67)	82 (54.67)	
65–74	54 (29.83)	919 (33.58)		42 (28.00)	42 (28.00)	
≥75	5 (2.76)	182 (6.65)		5 (3.33)	5 (3.33)	
Smoking history, n (%)			0.002			0.91
Yes	76 (41.99)	1,525 (55.72)		66 (44.00)	69 (46.00)	
No	104 (57.46)	1,199 (43.81)		83 (55.33)	80 (53.33)	
Unknown	1 (0.55)	13 (0.47)		1 (0.67)	1 (0.67)	
Alcohol intake history, n (%)			0.41			0.78
Yes	70 (38.67)	1,196 (43.70)		61 (40.67)	67 (44.67)	
No	110 (60.77)	1,530 (55.90)		88 (58.67)	82 (54.67)	
Unknown	1 (0.55)	11 (0.40)		1 (0.67)	1 (0.67)	
HER2 score, n (%)			<0.001			0.80
Negative	77 (42.54)	635 (23.20)		68 (45.33)	74 (49.33)	
Positive+	40 (22.10)	616 (22.51)		32 (21.33)	24 (16.00)	
Positive++	18 (9.94)	266 (9.72)		17 (11.33)	18 (12.00)	
Positive+++	13 (7.18)	178 (6.50)		9 (6.00)	11 (7.33)	
Unknown	33 (18.23)	1,042 (38.07)		24 (16.00)	23 (15.33)	
<i>H. pylori</i> infection, n (%)			0.06			0.69
Negative	22 (12.15)	200 (7.31)		18 (12.00)	19 (12.67)	
Positive	10 (5.52)	157 (5.74)		8 (5.33)	5 (3.33)	
Unknown	149 (82.32)	2,380 (86.96)		124 (82.67)	126 (84.00)	
Lauren, n (%)			<0.001			0.99
Diffuse type	56 (30.94)	318 (11.62)		47 (31.33)	47 (31.33)	
Intestinal type	34 (18.78)	768 (28.06)		32 (21.33)	34 (22.67)	
Mixed type	45 (24.86)	390 (14.25)		40 (26.67)	39 (26.00)	
Unknown	46 (25.41)	1,261 (46.07)		31 (20.67)	30 (20.00)	

Table 1 (continued)

Table 1 (continued)

Characteristics	Overall (N=2,918)			Propensity score matched (N=300) ¹		
	TG group (N=181)	PG group (N=2,737)	P value	TG group (N=150)	PG group (N=150)	P value
Histologic type, n (%)			<0.001			0.07
Well	7 (3.87)	149 (5.44)		4 (2.67)	3 (2.00)	
Moderately	24 (13.26)	827 (30.22)		23 (15.33)	11 (7.33)	
Poorly	140 (77.35)	1,668 (60.94)		123 (82.00)	136 (90.67)	
Undifferentiated, anaplastic	0	1 (0.04)		0	0	
Unknown	10 (5.52)	92 (3.36)				
Linitis plastica, n (%)			0.15			1.00
Yes	2 (1.10)	7 (0.26)		1 (0.67)	1 (0.67)	
No	179 (98.90)	2,716 (99.23)		149 (99.33)	149 (99.33)	
Unknown	0	14 (0.51)		–	–	
Nerve invasion, n (%)			<0.001			0.64
Yes	94 (51.93)	914 (33.39)		83 (55.33)	79 (52.67)	
No	85 (46.96)	1,793 (65.51)		67 (44.67)	71 (47.33)	
Unknown	2 (1.10)	30 (1.10)				
Vascular invasion, n (%)			0.006			0.93
Yes	83 (45.86)	948 (34.64)		68 (45.33)	71 (47.33)	
No	94 (51.93)	1,744 (63.72)		80 (53.33)	77 (51.33)	
Unknown	4 (2.21)	45 (1.64)		2 (1.33)	2 (1.33)	
pT, n (%)			0.24			0.02
T0	0	0		0	0	
T1	5 (2.76)	36 (1.32)		5 (3.33)	1 (0.67)	
T2	18 (9.94)	355 (12.97)		11 (7.33)	16 (10.67)	
T3	91 (50.28)	1,413 (51.63)		80 (53.33)	99 (66.00)	
T4	67 (37.02)	933 (34.09)		54 (36.00)	34 (22.67)	
pN, n (%)			0.04			0.08
N0	53 (29.28)	877 (32.04)		46 (30.67)	29 (19.33)	
N1	40 (22.10)	795 (29.05)		33 (22.00)	37 (24.67)	
N2	34 (18.78)	472 (17.25)		30 (20.00)	27 (18.00)	
N3	54 (29.83)	593 (21.67)		41 (27.33)	57 (38.00)	
pM, n (%)			–			–
M0	181 (100.00)	2,737 (100.00)		150 (100.00)	150 (100.00)	
M1	0	0		0	0	

Table 1 (continued)

Table 1 (continued)

Characteristics	Overall (N=2,918)			Propensity score matched (N=300) ¹		
	TG group (N=181)	PG group (N=2,737)	P value	TG group (N=150)	PG group (N=150)	P value
pTNM, n (%)			0.44			0.43
Ib	13 (7.18)	246 (8.99)		9 (6.00)	8 (5.33)	
II	67 (37.02)	1,089 (39.79)		59 (39.33)	49 (32.67)	
III	101 (55.80)	1,402 (51.22)		82 (54.67)	93 (62.00)	
Adjuvant therapies, n (%)			<0.001			0.45
Multimodality treatment	98 (54.14)	1,018 (37.19)		75 (50.00)	65 (43.33)	
Surgery only	10 (5.52)	258 (9.43)		9 (6.00)	8 (5.33)	
Unknown	73 (40.33)	1,461 (53.38)		66 (44.00)	77 (51.33)	
BMI, kg/m ² (mean ± SD)*	23.6±3.5	24.1±3.4	0.08	23.8±3.4	23.8±3.5	0.92
No. of lymph nodes metastasis, median [quantiles]*	2 [0–10]	2 [0–6]	0.02	2 [0–8]	4 [1–9]	0.07

*, some patients had missing values. ¹, Propensity score matched for gender, age, smoking, drinking, HER2 score, *H. pylori* infection, Lauren classification, histologic type, linitis plastica, nerve invasion, vascular invasion, pTNM, adjuvant therapies, BMI and no. of lymph nodes metastasis. TG, total gastrectomy; PG, proximal gastrectomy.

Secondly, surgeons from China National Cancer Center have enough ability to finish the technically demanding for PG surgery. Respect to clinicopathologic characteristics, we found TG patients appeared to more lymph node spread, nerve invasion, lymphatic vessel invasion and vascular invasion before propensity score matching, which was also observed in two published studies (17,24). This may a considerable factor for these patients underwent TG approach. Therefore, we performed a strict propensity match to eliminate the bias.

The extent of lymphadenectomy was a consideration when TG and PG are compared. Our study showed that the mean retrieved lymph nodes of TG group were ten lymph nodes more than that of PG group, which was in accordance with most studies targeting this issues (13,25–28). Therefore, TG did enable a more complete nodal dissection and it was apparent from the number of lymph nodes retrieved in the current study that TG did result in a somewhat better lymph node yield. Although TG can provide more complete lymphadenectomy, the correlation between clinical survival for LAPGC patients of these factors still needs further study. Yura *et al.* (29) following 202 LAPGC patients indicated that the metastatic rate of these lymph nodes was really low (#4d, 0.99%; #5, 0% and #6, 0%), while the nodes with high metastatic rate for

PGC, like #3, #2 and #1, were included in PG. This study also approved that oncological safety would be ensured by PG, without the need for TG when targeting for nodal dissection.

PG has long been thought to confer worse prognosis. A published study from Korea with 147 patients reported that individuals with pathological stage III gastric cardiac cancer, the 5-year survival of the TG was significantly higher than that of the PG group (38.4% *vs.* 17.1%, $P=0.04$) (24). Ying *et al.* compared the two groups for PGC patients with stage I–III and also demonstrated PG and TG groups had significantly different 5-year OS (45.2 *vs.* 50.9%, $P=0.047$) (19). However, a recent study for LAPGC patients including neoadjuvant chemotherapy revealed that the overall 2-year survival following PG and TG was 73.8% and 49.9%, respectively, and not statistically different ($P=0.10$), which might show the important role of chemotherapy for LAPGC patients survival outcomes (16). In our study, 3-, 5-year survival rates in PG group were slightly higher than ones in TG group, which might indicate that PG was a preferable approach for LAPGC patients. After propensity score matching in this study, a primary finding was that TG was not independently associated with OS when compared with PG even stratified by AJCC stage. Furthermore, PG was not a negative prognostic indicator in multivariate

Table 2 Comparison of surgical outcomes after propensity score matched

Surgical outcomes	TG group (N=150)	PG group (N=150)	P value
Surgical margin, n (%)			0.158
Negative	139 (92.67)	146 (97.33)	
Positive	9 (6.00)	3 (2.00)	
Unknown	2 (1.33)	1 (0.67)	
Operative approach, n (%)			<0.001
Open	104 (69.33)	146 (97.33)	
Laparoscopy-assisted	39 (26.00)	2 (1.33)	
Conversion to laparotomy	1 (0.67)	1 (0.67)	
Total laparoscopy	4 (2.67)	1 (0.67)	
Unknown	2 (1.33)	0	
Blood transfusion, n (%)			0.001
Yes	34 (22.67)	15 (10.00)	
No	94 (62.67)	123 (82.00)	
Unknown	22 (14.67)	12 (8.00)	
Postoperative mortality, n (%)			1.000
Yes	1 (0.67)	1 (0.67)	
No	148 (98.67)	148 (98.67)	
Unknown	1 (0.67)	1 (0.67)	
Estimated blood transfusion, mL, mean $\pm$ SD*	978.4 $\pm$ 421.1	743.8 $\pm$ 296.6	0.049
No. of retrieved lymph nodes, mean $\pm$ SD	34.3 $\pm$ 17.0	24.2 $\pm$ 11.0	<0.001
Operative time, min, mean $\pm$ SD*	213.5 $\pm$ 66.7	181.8 $\pm$ 49.8	<0.001
Postoperative stay, days, median [quantiles]*	12 [10–14]	11 [10–13]	0.644
Total expenses, yuan, median (quantiles)*	103,631.9 (87,613.2–127,005.8)	78,506.8 (71,550.6–97,969.2)	<0.001

*, some patients had missing values. TG, total gastrectomy; PG, proximal gastrectomy.

Table 3 Survival outcomes of LAPGC patients following PG and TG

The resection types	N	Mean of OS (95% CI)	3-year OS rate (%)	5-year OS rate (%)
LAPGC				
PG	150	158.8 (140.5–177.1)	79.1	74.5
TG	150	112.4 (102.0–122.8)	77.2	72.0
Stage II				
PG	49	157.7 (127.1–188.4)	91.0	85.7
TG	59	125.9 (112.2–139.6)	90.3	81.7
Stage III				
PG	93	155.7 (136.0–175.4)	73.3	68.8
TG	82	98.4 (83.1–113.7)	65.2	62.4

LAPGC: two stage hazard rate comparison, $P=0.2826$; 3- and 5-year OS rates: $P<0.0001$; Stage II: two stage hazard rate comparison, $P=0.3372$; 3-year OS rates: $P=0.36$; 5-year OS rates: $P<0.0001$; Stage III: log-rank chi-square =1.3760, $P=0.2408$; 3- and 5-year OS rates: $P<0.0001$. OS, overall survival; LAPGC, locally advanced proximal gastric cancer; PG, proximal gastrectomy; TG, total gastrectomy.

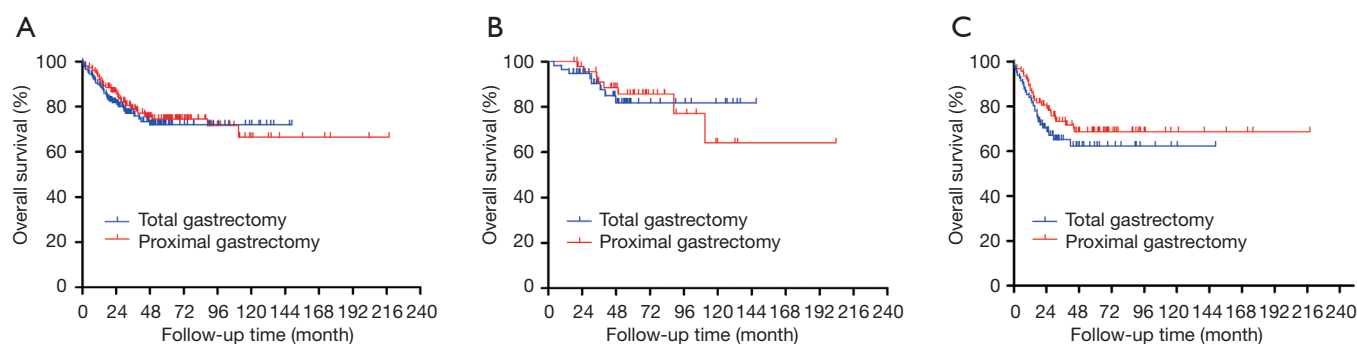


Figure 1 (A) Kaplan-Meier survival curves of LAPGC patients following PG and TG; (B) Kaplan-Meier survival curves of stage II LAPGC patients following PG and TG; (C) Kaplan-Meier survival curves of stage III LAPGC patients following PG and TG. LAPGC, locally advanced proximal gastric cancer; PG, proximal gastrectomy; TG, total gastrectomy.

Table 4 Predictor of OS on multivariate Cox regression analysis

Prognostic factors	Number	n, %	Unadjusted		Adjusted ¹	
			HR (95% CI)	P value	HR (95% CI)	P value
Gender						
Male	254	56 (22.0)	1		1	
Female	46	17 (37.0)	1.843 (1.071–3.173)	0.027	1.723 (0.832–3.571)	0.143
Age						
<50	42	15 (35.7)	1		1	
50–64	164	36 (22.0)	0.595 (0.325–1.086)	0.091	0.935 (0.473–1.849)	0.848
65–74	84	19 (22.6)	0.593 (0.301–1.166)	0.130	0.941 (0.433–2.046)	0.878
≥75	10	3 (30.0)	0.749 (0.217–2.587)	0.647	1.394 (0.354–5.482)	0.635
Smoking						
Yes	135	28 (20.7)	0.824 (0.512–1.326)	0.425	1.22 (0.640–2.324)	0.546
No	163	44 (27.0)	1		1	
Unknown	2	1 (50.0)	2.386 (0.327–17.429)	0.391	5.378 (0.467–62)	0.177
Drinking						
Yes	128	27 (21.1)	0.82 (0.509–1.324)	0.418	1.165 (0.618–2.196)	0.636
No	170	45 (26.5)	1		1	
Unknown	2	1 (50.0)	2.391 (0.328–17.449)	0.390	–	–
HER2 score						
Negative	142	29 (20.4)	1		1	
Positive+	56	11 (19.6)	0.943 (0.471–1.889)	0.869	1.415 (0.680–2.941)	0.353
Positive++	35	7 (20.0)	0.949 (0.416–2.168)	0.902	0.929 (0.360–2.398)	0.879
Positive+++	20	9 (45.0)	2.656 (1.256–5.616)	0.011	5.038 (2.164–11.725)	0.000
Unknown	47	17 (36.2)	1.435 (0.777–2.652)	0.249	0.958 (0.378–2.428)	0.927

Table 4 (continued)

Table 4 (continued)

Prognostic factors	Number	n, %	Unadjusted		Adjusted ¹	
			HR (95% CI)	P value	HR (95% CI)	P value
<i>H. pylori</i> infection						
Negative	37	3 (8.1)	1		1	
Positive	13	3 (23.1)	3.701 (0.746–18.361)	0.109	9.453 (1.555–57.467)	0.015
Unknown	250	67 (26.8)	3.408 (1.072–10.839)	0.038	3.543 (0.924–13.585)	0.065
Lauren						
Intestinal type	66	8 (12.1)	1		1	
Diffuse type	94	27 (28.7)	2.636 (1.197–5.803)	0.016	2.218 (0.905–5.439)	0.082
Mixed type	79	16 (20.3)	1.822 (0.779–4.257)	0.166	1.620 (0.649–4.045)	0.301
Unknown	61	22 (36.1)	2.553 (1.127–5.782)	0.025	3.964 (1.322–11.885)	0.014
Histologic type						
Well	7	0				
Moderately	34	5 (14.7)	1		1	
Poorly	259	68 (26.3)	1.969 (0.794–4.885)	0.144	1.952 (0.688–5.537)	0.209
Linitis plastica						
Yes	2	2 (100.0)	15.025(3.522–64.107)	<0.001	10.263 (1.896–55.557)	0.007
No	298	71 (23.8)	1		1	
Nerve invasion						
Yes	162	37 (22.8)	1.018 (0.639–1.621)	0.940	1.145 (0.656–1.998)	0.634
No	138	36 (26.1)	1		1	
Vascular invasion						
Yes	139	34 (24.5)	1.115 (0.701–1.773)	0.646	0.737 (0.431–1.262)	0.267
No	157	38 (24.2)	1		1	
Unknown	4	1 (25.0)	1.350 (0.185–9.87)	0.767	1.258 (0.136–11.655)	0.840
pTNM						
I	17	2 (11.8)	0.855 (0.196–3.72)	0.834	0.878 (0.188–4.105)	0.869
II	108	16 (14.8)	1		1	
III	175	55 (31.4)	2.651 (1.518–4.632)	0.001	2.621 (1.415–4.855)	0.002
Surgical margin						
Negative	285	67 (23.5)	1		1	
Positive	12	4 (33.3)	1.559 (0.568–4.277)	0.389	0.986 (0.31–3.138)	0.981
Unknown	3	2 (66.7)	2.468 (0.603–10.096)	0.209	3.032 (0.588–15.632)	0.185
Surgery type						
PG	150	37 (24.7)	1		1	
TG	150	36 (24.0)	1.060 (0.842–1.334)	0.620	1.172 (0.916–1.499)	0.208

¹, Adjust for gender, age, smoking, drinking, HER2, *H. pylori* infection, Lauren, histologic type, plastica, nerve invasion, vascular invasion, TNM, surgical margin, complex therapies and surgery type. OS, overall survival; PG, proximal gastrectomy; TG, total gastrectomy.

analysis.

Strengths and limitations should be considered when interpreting the study results. One limitation of this study was that it was retrospective and just conducted in a single institution, so the results might not represent the whole Chinese population. The second limitation was that postoperative function and patient quality of life following PG or TG was neither evaluated nor documented well. The study also had several strengths. Firstly, to date, this cohort was the largest to compare the long-term survival outcomes between PG and TG. Secondly, we used a propensity score matching analysis to reduce bias, which was considered to mimic randomized controlled trials.

Conclusions

In conclusion, the extent of resection for LAPGC patients did not influence the long-term OS outcomes. Moreover, future randomized clinical trials of quality of life following PG or TG are expected to assist surgeons in the choice of surgical approach and strategy for LAPGC patients.

Acknowledgments

Funding: All authors made substantial contributions to the intellectual content of this paper. This study was funded in part by the National Key R&D Program of China (Grant No.2017YFC0908300).

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2020.02.38>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the ethics committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 17-156/1412). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

Open Access Statement: This is an Open Access article

distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer* 2019;144:1941-53.
2. Deans C, Yeo MS, Soe MY, et al. Cancer of the gastric cardia is rising in incidence in an Asian population and is associated with adverse outcome. *World J Surg* 2011;35:617-24.
3. Carr JS, Zafar SE, Saba N, et al. Risk factors for rising incidence of esophageal and gastric cardia adenocarcinoma. *J Gastrointest Cancer* 2013;44:143-51.
4. Steevens J, Botterweck AA, Dirx MJ, et al. Trends in incidence of oesophageal and stomach cancer subtypes in Europe. *Eur J Gastroenterol Hepatol* 2010;22:669-78.
5. Crew KD, Neugut AI. Epidemiology of gastric cancer. *World J Gastroenterol* 2006;12:354-62.
6. An JY, Youn HG, Choi MG, et al. The difficult choice between total and proximal gastrectomy in proximal early gastric cancer. *Am J Surg* 2008;196:587-91.
7. Kitamura K, Yamaguchi T, Okamoto K, et al. Total gastrectomy for early gastric cancer. *J Surg Oncol* 1995;60:83-8.
8. Kaibara N, Nishimura O, Nishidoi H, et al. Proximal gastrectomy as the surgical procedure of choice for upper gastric carcinoma. *J Surg Oncol* 1987;36:110-2.
9. Ikeguchi M, Kader A, Takaya S, et al. Prognosis of patients with gastric cancer who underwent proximal gastrectomy. *Int Surg* 2012;97:275-9.
10. Nozaki I, Hato S, Kobatake T, et al. Long-term outcome after proximal gastrectomy with jejunal interposition for gastric cancer compared with total gastrectomy. *World J Surg* 2013;37:558-64.
11. Ichikawa D, Komatsu S, Kubota T, et al. Long-term outcomes of patients who underwent limited proximal gastrectomy. *Gastric Cancer* 2014;17:141-5.
12. Isobe T, Hashimoto K, Kizaki J, et al. Reconstruction methods and complications in proximal gastrectomy for

- gastric cancer, and a comparison with total gastrectomy. *Kurume Med J* 2014;61:23-9.
13. Son MW, Kim YJ, Jeong GA, et al. Long-term outcomes of proximal gastrectomy versus total gastrectomy for upper-third gastric cancer. *J Gastric Cancer* 2014;14:246-51.
 14. Hosoda K, Yamashita K, Katada N, et al. Potential benefits of laparoscopy-assisted proximal gastrectomy with esophagogastrostomy for cT1 upper-third gastric cancer. *Surg Endosc* 2016;30:3426-36.
 15. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011;14:113-23.
 16. Sugo P, Shah S, Dusane R, et al. Proximal gastrectomy versus total gastrectomy for proximal third gastric cancer: total gastrectomy is not always necessary. *Langenbecks Arch Surg* 2016;401:687-97.
 17. Rosa F, Quero G, Fiorillo C, et al. Total vs proximal gastrectomy for adenocarcinoma of the upper third of the stomach: a propensity-score-matched analysis of a multicenter western experience (On behalf of the Italian Research Group for Gastric Cancer-GIRCG). *Gastric Cancer* 2018;21:845-52.
 18. Zhao D, Xu H, Li K, et al. Prognostic factors for patients after curative resection for proximal gastric cancer. *J Huazhong Univ Sci Technolog Med Sci* 2010;30:530-5.
 19. Ying KM, Chen Z, Dang CX, et al. Clinicopathology and survival in patients with gastroesophageal reflux after radical surgery of proximal gastric cancer. *Dig Dis Sci* 2018;63:1035-42.
 20. Qiu P, Sheng J. A two-stage procedure for comparing hazard rate functions. *J R Stat Soc Series B Stat Methodol* 2008;70:191-208.
 21. Erturk MS, Çiçek Y, Ersan Y, et al. Analysis of clinicopathological prognostic parameters in adenocarcinoma of the gastric cardia. *Acta Chir Belg* 2003;103:611-5.
 22. Yoo CH, Sohn BH, Han WK, et al. Long-term results of proximal and total gastrectomy for adenocarcinoma of the upper third of the stomach. *Cancer Res Treat* 2004;36:50-5.
 23. Harrison LE, Karpeh MS, Brennan MF. Total gastrectomy is not necessary for proximal gastric cancer. *Surgery* 1998;123:127-30.
 24. Kim JH, Park SS, Kim J, et al. Surgical outcomes for gastric cancer in the upper third of the stomach. *World J Surg* 2006;30:1870-6; discussion 1877-8.
 25. Hayami M, Hiki N, Nunobe S, et al. Clinical outcomes and evaluation of laparoscopic proximal gastrectomy with double-flap technique for early gastric cancer in the upper third of the stomach. *Ann Surg Oncol* 2017;24:1635-42.
 26. Kosuga T, Ichikawa D, Komatsu S, et al. Feasibility and nutritional benefits of laparoscopic proximal gastrectomy for early gastric cancer in the upper stomach. *Ann Surg Oncol* 2015;22 Suppl 3:S929-35.
 27. Jung DH, Lee Y, Kim DW, et al. Laparoscopic proximal gastrectomy with double tract reconstruction is superior to laparoscopic total gastrectomy for proximal early gastric cancer. *Surg Endosc* 2017;31:3961-9.
 28. Yoo CH, Sohn BH, Han WK, et al. Proximal gastrectomy reconstructed by jejunal pouch interposition for upper third gastric cancer: prospective randomized study. *World J Surg* 2005;29:1592-9.
 29. Yura M, Yoshikawa T, Otsuki S, et al. Oncological safety of proximal gastrectomy for T2/T3 proximal gastric cancer. *Gastric Cancer* 2019;22:1029-35.

Cite this article as: Zhao L, Ling R, Ma F, Ren H, Zhou H, Wang T, Chen Y, Hu S, Zhao D. Clinical outcomes of proximal gastrectomy versus total gastrectomy for locally advanced proximal gastric cancer: a propensity score matching analysis. *Transl Cancer Res* 2020;9(4):2769-2779. doi: 10.21037/tcr.2020.02.38

Supplementary

Table S1 Multivariate analysis between different groups in II stage

Prognostic factors	Number	n, %	Unadjusted		Adjusted ¹	
			HR (95% CI)	P value	HR (95% CI)	P value
The resection types						
PG	49	8 (16.3)	1		1	
TG	59	8 (13.6)	1.015 (0.621–1.659)	0.952	1.329 (0.713–2.478)	0.371

¹, adjust for gender, age, smoking, drinking, HER2 score, *H. pylori* infection, Lauren classification, histologic type, linitis plastica, nerve invasion, vascular invasion, pTNM stage, surgical margin, adjuvant therapies. PG, proximal gastrectomy; TG, total gastrectomy.

Table S2 Multivariate analysis between different groups in III stage

Prognostic factors	Number	n, %	Unadjusted		Adjusted ¹	
			HR (95% CI)	P value	HR (95% CI)	P value
The resection types						
PG	93	27 (29.0)	1		1	
TG	82	28 (34.1)	1.171 (0.898–1.528)	0.243	1.196 (0.889–1.608)	0.236

¹, adjust for gender, age, smoking, drinking, HER2 score, *H. pylori* infection, Lauren classification, histologic type, linitis plastica, nerve invasion, vascular invasion, pTNM stage, surgical margin, adjuvant therapies. PG, proximal gastrectomy; TG, total gastrectomy.