Retrospective Cohort Study

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Total versus proximal gastrectomy for proximal gastric cancer after neoadjuvant chemotherapy: a multicenter retrospective propensity score-matched cohort study

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Background: This study aimed to analyze and compare the short-term and long-term outcomes of proximal gastrectomy (PG) and total gastrectomy (TG) in patients with locally advanced proximal gastric cancer (GC) following neoadjuvant chemotherapy (NACT).
Method: A multicenter retrospective cohort study and propensity score matching (PSM) were employed. The authors examined 367 patients with proximal GC who received NACT followed by PG ($n = 164$) or TG ($n = 203$) at two Chinese medical institutions between December 2009 and December 2022. Clinical and pathological parameters, postoperative complications, and 5-year overall survival (OS) and recurrence-free survival (RFS) were compared between the two groups. The dissection status and metastasis rate of each lymph node station were assessed.
Results: After PSM, 80 patients were enrolled in both TG and PG group, and baseline characteristics were comparable between the groups (all $P > 0.05$). The TG group had a higher total number of lymph nodes retrieved ($P < 0.001$) and longer operative time ($P = 0.007$) compared to the PG group. The incidence of Clavien–Dindo grade II or higher postoperative complications was similar between the TG group (21.3%, 17/80) and the PG group (17.5%, 14/80) ($P = 0.689$). The 5-year OS rates were 68.4 for the PG group and 66.0% for the TG group ($P = 0.881$), while the 5-year RFS rates were 64.8 and 61.9%, respectively ($P = 0.571$), with no statistically significant differences. Metastasis rates at lymph node stations #4d, #5, #6, and #12a were notably low in the TG group, with values of 2.74, 0.67, 1.33, and 1.74%, respectively.
Conclusion: For proximal GC patients following NACT, PG maintains comparable curative potential and oncological efficacy to TG, making it a safe option.

Keywords: neoadjuvant chemotherapy, proximal gastrectomy, proximal gastric cancer, total gastrectomy

Introduction

Gastric cancer (GC) remains a formidable global health challenge, with a substantial burden of morbidity and mortality[1]. The incidence of GC varies geographically, with a particularly high prevalence in Eastern Asia[2]. Among GC cases, proximal GC, defined as tumors located in the upper third of the stomach, represents a distinct subset[3]. Over the past two decades, the

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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proportion of tumors located in the upper one-third of the stomach has increased from 5.3 to 14.0%[4], and the cancer-related mortality rate in this region is significantly higher than that in other parts of the stomach[5]. The management of proximal GC poses unique clinical and surgical challenges, necessitating the development of tailored therapeutic strategies to optimize patient outcomes.

Neoadjuvant chemotherapy (NACT) has emerged as a valuable component of the multidisciplinary approach to GC treatment, offering the potential to downstage tumors, increase the likelihood of curative resection, and improve long-term survival[6,7]. In particular, NACT has been explored as a viable strategy for patients with locally advanced proximal GC, aiming to enhance the feasibility of surgical resection and reduce the extent of surgery required[8–10]. However, the optimal surgical approach for patients who have undergone NACT remains a subject of debate, particularly concerning the choice between proximal gastrectomy (PG) and total gastrectomy (TG).

PG and TG represent two major surgical approaches for the treatment of proximal GC[11,12]. PG involves the resection of the proximal stomach with preservation of the distal remnant, while TG entails the complete removal of the stomach[13]. Each procedure has its unique advantages and limitations. PG offers the potential for functional preservation by retaining a portion of the stomach, potentially reducing postoperative complications such as malabsorption and dumping syndrome[14,15]. In contrast, TG provides extensive lymphadenectomy and may be associated with improved oncological outcomes, particularly for patients with advanced proximal GC[16].

The choice between PG and TG in the context of NACT has significant implications for both short-term postoperative recovery and long-term oncological results. To date, there is a paucity of comprehensive evidence comparing these two surgical approaches specifically in the setting of proximal GC patients who have received NACT. Previous studies have predominantly focused on proximal GC without considering the impact of neoadjuvant therapy[11,12,14,17].

In light of this, we conducted a multicenter retrospective cohort study and employed propensity score matching (PSM) to analyze and compare the outcomes of PG and TG in patients with locally advanced proximal GC who received NACT. Our study aimed to assess short-term surgical outcomes, long-term survival, and the therapeutic value of key distal lymph node dissection in these patients, with the goal of providing valuable insights into the selection of the most appropriate surgical approach.

HIGHLIGHTS

- We assessed the surgical approaches selection in proximal GC patients post-neoadjuvant chemotherapy.
- Proximal gastrectomy (PG) and total gastrectomy (TG) yield comparable rates of R0 resection and postoperative complications.
- PG shows parallel 5-year overall survival and 5-year recurrence-free survival compared to TG.
- Notably low metastasis rates at un-dissected nodes (#4d, #5, #6, and #12a) in PG.

Material and methods

Study design and participants

The study flow diagram is shown in Figure 1. This retrospective study collected clinical data from patients who were enrolled at the Chinese PLA General Hospital (n = 287) and the First Affiliated Hospital of Army Medical University (n = 80). The hospital information was concealed during submission for blind review. A total of 164 and 203 patients underwent PG and TG, respectively. The inclusion criteria were as follows: (1) patients diagnosed with locally advanced GC with tumors located in the upper third of the stomach without esophagogastric junction adenocarcinomas; (2) tumor stage ranging from TNM stage I to III, with no evidence of distant metastases; (3) patients who underwent at least two cycles of NACT followed by minimally invasive radical gastrectomy (laparoscopic or robotic surgery); (4) American Society of Anesthesiology (ASA) score of class I, II, or III. The exclusion criteria were as follows: (1) patients previously diagnosed with GC; (2) emergency surgery; (3) conversion to laparotomy.

A total of 93 patients were excluded from subsequent analysis for the following reasons: distant metastases (n = 27), emergency surgery (n = 10), incomplete data (n = 34), less than two cycles of NACT (n = 15), and prior history of endoscopic submucosal dissection (n = 7). Therefore, a total of 274 patients with upper third GC were included in the analysis. All patients were followed up until the last contact or death occurred. The follow-up was conducted until 1 September 2023. The median duration of follow-up was 55.8 months [interquartile range (IQR), 25.8–76.2 months]. This work has been reported in line with the strengthening the reporting of cohort, cross-sectional and case–control studies in surgery (STROCSS) criteria[18] (Supplemental Digital Content 1, http://links.lww.com/JS9/B500).

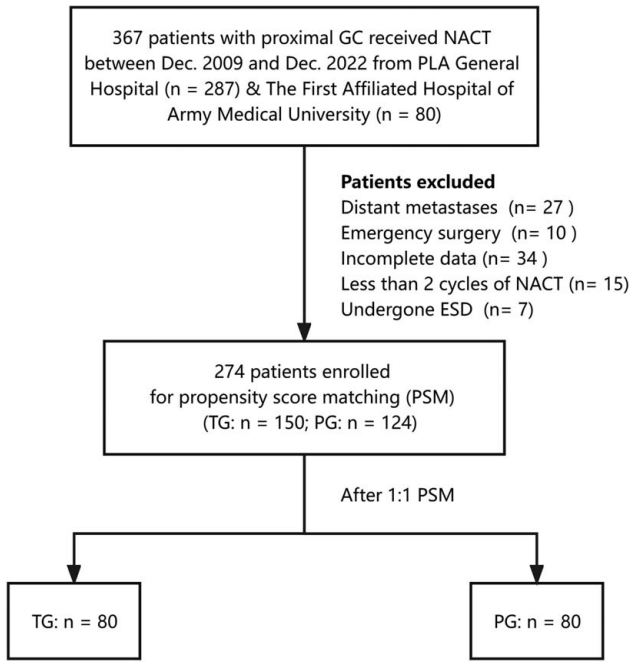

Figure 1. Flowchart of the study population. ESD, endoscopic submucosal dissection; GC, gastric cancer; NACT, neoadjuvant chemotherapy; PG, proximal gastrectomy; TG, total gastrectomy.

Table 1

Clinical characteristics of patients after propensity score matching.

	PG	TG	
	(*N* = 80)	(*N* = 80)	*P*
Sex, *n* (%)			
Female	10 (12.5)	12 (15.0)	0.818
Male	70 (87.5)	68 (85.0)	
Age[a], years	63.0 (58.0–68.0)	64.0 (57.8–68.3)	0.876
Approach, *n* (%)			
Laparoscopic	58 (72.5)	64 (80.0)	0.353
Robotic	22 (27.5)	16 (20.0)	
Blood loss[a], ml	200 (100–300)	150 (100–200)	0.208
Operative time[a], min	220 (180–270)	250 (210–300)	0.007
ASA score, *n* (%)			
1–2	69 (86.3)	68 (85.0)	1.000
3	11 (13.8)	12 (15.0)	
CCI score, *n* (%)			
≤ 2	22 (27.5)	26 (32.5)	0.605
> 2	58 (72.5)	54 (67.5)	
BMI[a], kg/m2	23.1 (21.1–25.9)	22.9 (21.1–25.3)	0.412
Hospitalization[a], days	10.0 (8.00–12.0)	10.0 (8.00–14.0)	0.850
TRG, *n* (%)			
0	6 (7.5)	5 (6.3)	0.883
1	14 (17.5)	15 (18.8)	
2	33 (41.3)	29 (36.3)	
3	27 (33.8)	31 (38.8)	
Lymph nodes retrieved[a], *n*	25.0 (21.0–30.0)	34.0 (27.0–44.0)	< 0.001
ypT stage, *n* (%)			
0–1	16 (20.0)	13 (16.3)	0.736
2	17 (21.3)	14 (17.5)	
3	36 (45.0)	38 (47.5)	
4	11 (13.8)	15 (18.8)	
ypN stage, *n* (%)			
0	45 (56.3)	40 (50.0)	0.775
1	15 (18.8)	14 (17.5)	
2	7 (8.8)	12 (15.0)	
3a	10 (12.5)	10 (12.5)	
3b	3 (3.8)	4 (5.0)	
ypTNM stage, *n* (%)			
0	4 (5.0)	4 (5.0)	0.766
1	27 (33.8)	21 (26.3)	
2	26 (32.5)	28 (35.0)	
3	23 (28.8)	27 (33.8)	
Tumor size[a], mm	30.0 (15.0–46.3)	30.6 (21.2–50.0)	0.590
Differentiation, *n* (%)			
Poor/Other types	44 (55.0)	43 (53.8)	1.000
Well/moderate	36 (45.0)	37 (46.3)	
Resection, *n* (%)			
R0	79 (98.8)	78 (97.5)	1.000
R1/R2	1 (1.3)	2 (2.5)	
NACT cycles, *n* (%)			
2	21 (26.3)	21 (26.3)	0.994
3	14 (17.5)	15 (18.8)	
4	34 (42.5)	34 (42.5)	
> 4	11 (13.8)	10 (12.5)	
NACT regimen, *n* (%)			
SOX	50 (62.5)	52 (65.0)	0.953
DOS	4 (5.0)	5 (6.3)	
XELOX	19 (23.8)	17 (21.3)	
Other	7 (8.8)	6 (7.5)	
Adjuvant chemotherapy, *n* (%)	54 (67.5)	52 (65.0)	0.867
Perineural invasion, *n* (%)	12 (15.0)	14 (17.5)	0.830
Vascular invasion, *n* (%)	15 (18.8)	18 (22.5)	0.696

[a]Values are presented as median (Q1-Q3).

ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; NACT, Neoadjuvant chemotherapy treatment; PG, proximal gastrectomy; TG, total gastrectomy; TRG, Tumor regression grade.

NACT regimens and surgical procedures

All patients have received at least two cycles of NACT. The NACT regimens included SOX (102/160, 63.8%), DOS (9/160, 5.6%), XELOX (36/160, 22.5%), and other regimens (13/160, 8.1%, including TP, FLOT, FOLFOX, and DF). The selection of TG or PG combined with D2 lymphadenectomy was determined based on a comprehensive assessment of factors, including tumor regression grade (TRG), tumor size, tumor location, and patient preferences. In the TG group, the gastrointestinal reconstruction involved Roux-en-Y anastomosis, whereas in the PG group, gastrointestinal reconstruction encompassed tube-type gastric anastomosis, double-channel anastomosis, and anastomosis of the posterior wall of the residual stomach. All surgical procedures were performed by proficient chief surgeons with extensive experience.

Outcomes and definitions

The primary outcome was overall survival (OS), calculating from the date of surgery to the date of death caused by any reasons or the most recent follow-up. The secondary outcomes were recurrence-free survival (RFS) and postoperative complications. RFS calculated from the date of surgery to the date of recurrence (at any site) or the most recent follow-up. The evaluation of TRG from 0 to 3 was classified as follows according to NCCN[19]: 0 (complete response), 1 (moderate response), 2 (minimal response), or 3 (poor response). Postoperative morbidity was assessed with Clavien–Dindo classification[20]. The assessment of resection margins and ypTNM stage were carried out according to the 8th edition of AJCC/UICC classification[21]. The differentiation types comprised well/moderate and poor/other types, with the latter encompassing poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous adenocarcinoma.

Therapeutic value index calculation

To assess the therapeutic impact of lymph node dissection at each nodal station, we utilized the therapeutic value index as initially proposed by Sasako *et al.*[22]. The therapeutic value index for lymph node dissection was derived by multiplying the rate of lymph node metastasis by the corresponding 5-year OS rate. Lymph node metastasis rate was determined by multiplying the number of patients with lymph node metastasis at each nodal station by the total number of patients from whom that station was retrieved. Five year OS rate among patients with LN metastasis was calculated separately for each nodal station.

Statistical analysis

The PSM was conducted to match the potential bias of confounding covariates between the two groups. The following factors were used for matching: sex, age, approach, ASA score, CCI score, BMI, ypT stage, ypN stage, ypTNM stage, tumor size, differentiation, resection, NACT cycles, NACT regimen, perineural invasion and vascular invasion. To maximize the utilization of data, 1:1 nearest neighbor caliper matching without replacement was performed with a caliper value of 0.02.

χ^2-tests or the Fisher exact test was used to compare categorical variables between TG and PG groups, while the Wilcoxon rank test or Student's *t*-test was used for continuous variables. OS and RFS curves were generated using Kaplan–Meier (K–M) estimates. Hazard ratios (HRs) and 95% CIs were calculated using Cox proportional hazards regression models. Univariate Cox

regression analysis and multivariate Cox regression analysis were conducted to assess factors associated with OS and RFS. Variables with P values less than 0.05 in the univariate Cox analysis were included in the multivariate Cox analysis. A forest plot was utilized to visualize the results of the multivariate Cox analysis.

All analyses were performed using R 4.2.2. All P values were based on a two-sided hypothesis, and those less than 0.05 were considered statistically significant.

Results

Patient characteristics

The flowchart shows in Figure 1. Two hundred seventy-four patients met the criteria were enrolled in the study, and 160 patients were enrolled in the analysis after PSM. Of these, 80 and 80 patients underwent TG and PG, respectively. Table 1 summarize the clinicopathological characteristics after PSM. Overall, no significant difference was found in TRG, ypTNM stage, differentiation, gastrectomy approach, NACT cycles and NACT regimens. However, the TG group had a higher total number of lymph nodes retrived [TG, 34 (IQR, 27–44) vs. PG, 25 (IQR, 21–30); $P < 0.001$] and longer operative time [TG, 250 (IQR, 210–300) vs. PG, 220 (IQR, 180–270); $P = 0.007$] compared to the PG group. TRG 0 and 1 were 7.5% (6/80) and 17.5% (14/80) in PG group, and it was 6.3% (5/80) and 18.8% (15/80) in TG group. The rate of patients received at least four cycles of NACT were 56.3% (45/80) and 55.0% (44/80) in PG and TG group, respectively. The rate of administration in NACT of SOX, XELOX and DOS in PG and TG were 62.5, 23.8, 5.0% and 65.0, 21.3, 6.3%. There was no statistically significant difference in NACT regimens between the two groups ($P = 0.953$).

Postoperative complications

Postoperative morbidity in each group are shown in Table 2. There was no significant difference in the occurrence of Clavien–Dindo grade II or higher complications between the two groups (PG vs. TG, 17.5 vs. 21.3%, $P = 0.689$). In the PG group, the most common postoperative complications observed are bleeding (5.0%, 4/80) and anastomotic fistula (3.8%, 3/80), whereas in the control group, the most prevalent complications are bleeding (3.8%, 3/80) and pneumonia (3.8%, 3/80).

Recurrence and survival

The median follow-up interval was 55.8 (IQR, 25.8–76.2) months. Figure 2 shows the K–M analysis for OS and RFS stratified by surgical procedure. The 5-year of OS rates were 68.4 and 66.0% in PG and TG group ($P = 0.881$). The 5-year of RFS rates were 64.8 and 61.9% in PG and TG group ($P = 0.571$). Furthermore, we also conducted subgroup survival analysis stratified by ypTNM stage (Fig. S1, Supplemental Digital Content 2, http://links.lww.com/JS9/B501). Subgroup analysis results revealed that for ypTNM stage I patients, the PG group exhibited a 5-year OS advantage over the TG group (91.0 vs. 85.7%, $P = 0.036$); however, for ypTNM stage II–III patients, no statistically significant differences were observed in 5-year OS and 5-year RFS between the two groups (all $P > 0.05$).

Univariate Cox regression analysis was conducted to assess the association between individual factors and OS (Fig. 3) and RFS (Fig. S2, Supplemental Digital Content 2, http://links.lww.com/JS9/B501). The analysis revealed that lower ypT stage (HR = 2.06, 95% CI: 1.02–4.14, $P = 0.042$) and lower ypN stage (HR = 1.94, 95% CI: 1.07–3.51, $P = 0.028$) were significantly associated with worse OS, and lower ypN stage (HR = 2.11, 95% CI: 1.18–3.78, $P = 0.012$) and larger tumor size (HR = 1.74, 95% CI: 1.00–3.03, $P = 0.049$) were associated with worse RFS. The surgical resection procedure (TG or PG), was not found to be an independent prognostic risk factor in the analysis.

Table 2

Postoperative morbidity in each procedure.

	PG (*N* = 80)	TG (*N* = 80)	*P*
Postoperative morbidity (C–D grade ≥ II), *n* (%)			
Present	14 (17.5)	17 (21.3)	0.689
Absent	66 (82.5)	63 (78.8)	
Adverse event (C–D grade ≥ II), *n* (%)			
Anastomotic fistula	3 (3.8)	2 (2.5)	1.000
Bleeding	4 (5.0)	3 (3.8)	1.000
Heart failure	1 (1.3)	2 (2.5)	1.000
Intrabdominal abscess	1 (1.3)	2 (2.5)	1.000
Pancreatic fistula	2 (2.5)	0	0.477
Pleural effusion	1 (1.3)	2 (2.5)	1.000
Pneumonia	1 (1.3)	3 (3.8)	0.613
Respiratory failure	1 (1.3)	1 (1.3)	1.000
Liver dysfunction	0	1 (1.3)	1.000

PG, proximal gastrectomy; TG, total gastrectomy.

Therapeutic value of each nodal station

The lymph node metastasis patterns of patients received TG are presented in Table 3. According to the 6th edition of the Japanese GC Treatment Guidelines[23], the primary distinction in lymph node dissection between TG and PG lies in the clearance of critical distant lymph nodes: #4d (right greater curvature nodes along the right gastroepiploic artery), #5 (suprapyloric nodes), #6 (infrapyloric nodes), and #12a (nodes along the proper hepatic artery). The metastasis rates for #4d, #5, #6, and #12a were 2.74% (4/146), 0.67% (1/150), 1.33% (2/150), and 1.74% (2/115), respectively. Therefore, the therapeutic value index for #4d, #5, #6, and #12a were 1.55, 2.33, 1.59 and 0, respectively. When stratified by TRG, the metastasis rates for #4d, #5, #6, and #12a in TRG0/1 patients were all 0, while in TRG2 patients, the rates were 1.85% (1/54), 0% (0/54), 1.85% (1/54), and 0% (0/37), respectively. In TRG3 patients, the metastasis rates were 5.55% (3/54), 1.72% (1/58), 1.72% (1/58), and 4.08% (2/49) for #4d, #5, #6, and #12a, respectively. The highest metastasis rates were observed in lymph nodes #3 (24.67%, 37/150), #1 (24.00%, 36/150), #2 (14.00%, 21/150), and #7 (12.33%, 18/146).

Discussion

This study contributes valuable insights into the surgical management of proximal GC patients who have undergone NACT. Our comprehensive analysis of postoperative complications, specifically Clavien–Dindo grade II or higher, reveals no statistically significant differences between PG and TG. Furthermore, we find no notable distinctions in terms of R0 resection rates or 5-year OS and RFS. These findings underscore the safety profile

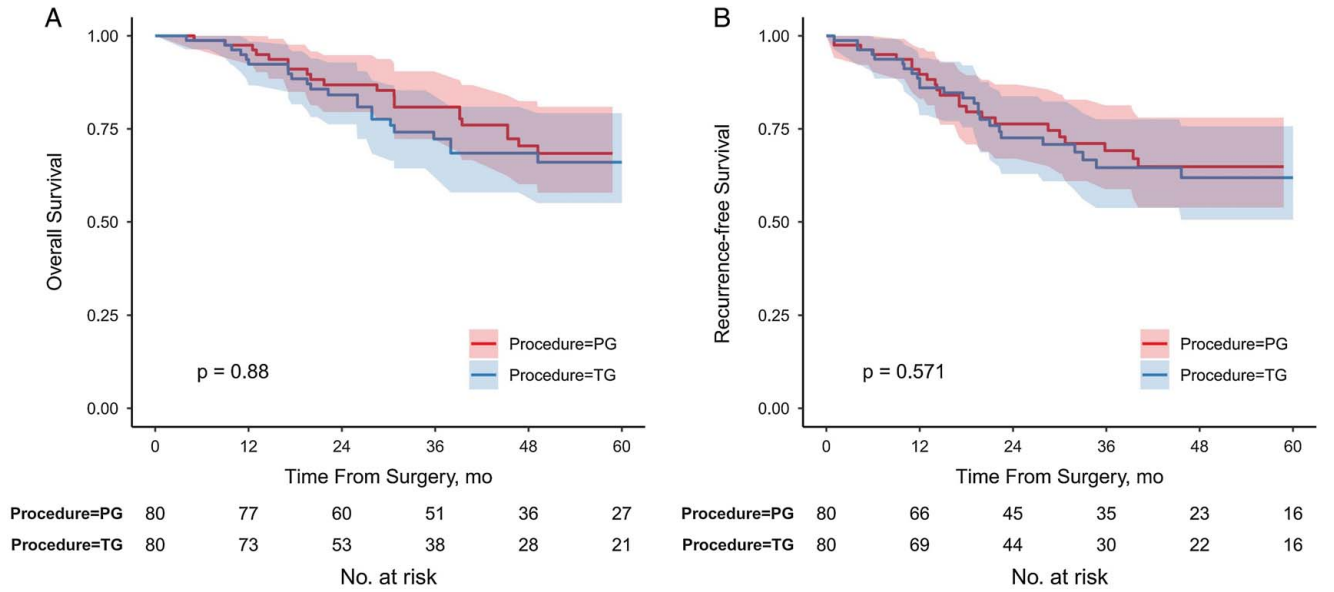

Figure 2. Kaplan–Meier estimates of overall survival (A) and recurrence-free survival (B) stratified by surgical procedure. PG, proximal gastrectomy; TG, total gastrectomy.

of PG, highlighting its potential as a compelling alternative to the more complex TG procedure. To our knowledge, this represents the largest retrospective multicenter study on postoperative complications and long-term outcomes in proximal GC patients after NACT.

Currently, most studies support no difference in short-term and long-term efficacy between PG and TG for patients with proximal GC undergone surgical treatment directly. The latest Japanese GC Treatment Guidelines also recommend PG for tumors of the upper stomach less than 40 mm in diameter[23]. Rosa *et al.*[11] reported that postoperative complication rates after PG and TG were 25.3 and 28% in adenocarcinoma of the upper third of the stomach, respectively ($P = 0.084$), and 5-year OS for PG and TG group was 56.7 and 46.5%, respectively ($P = 0.07$). Sugoor *et al.*[24]reported that there was no statistical difference observed in the distal resection margin positivity rates (PG = 4.7%, TG = 3.1%), and the overall 2-year survival following PG and TG was 73.8 and 49.9%, respectively. However, few studies have assessed short-term and long-term outcomes comparing these surgical procedures for proximal GC patients undergoing NACT.

Additionally, subgroup analysis indicated better 5-year survival with PG over TG for ypTNM stage I patients. This generally agrees with Yamasaki's retrospective study[14], which also found comparable 3-year OS and RFS between PG and TG for patients with cT1N0M0 GC limitedly located in the upper gastric body. Considering our limited ypTNM stage I sample, this finding warrants expanded validation. But it indicates functional

Table 3

Incidence of lymph node metastasis, 5-year OS rate and therapeutic index in patients received total gastrectomy ($n = 150$).

	Metastatic rate (%)					
Station no.	TRG0/1 ($n = 38$)	TRG 2 ($n = 54$)	TRG 3 ($n = 58$)	Total ($n = 150$)	5-year OS (%)	Therapeutic index
1	3/38 (7.89)	11/54 (20.37)	22/58 (37.93)	36/150 (24.00)	64.50	15.48
2	2/38 (5.26)	4/54 (7.41)	15/58 (25.86)	21/150 (14.00)	60.20	8.43
3	0/38 (0.00)	15/54 (27.78)	22/58 (37.93)	37/150 (24.67)	65.00	16.04
4sa	0/38 (0.00)	4/54 (7.41)	5/58 (8.65)	9/150 (6.00)	61.70	3.70
4sb	0/38 (0.00)	3/54 (5.55)	4/58 (6.9)	7/150 (4.67)	38.60	1.80
4d	0/38 (0.00)	1/54 (1.85)	3/54 (5.55)	4/146 (2.74)	56.70	1.55
5	0/38 (0.00)	0/54 (0.00)	1/58 (1.72)	1/150 (0.67)	58.20	2.33
6	0/38 (0.00)	1/54 (1.85)	1/58 (1.72)	2/150 (1.33)	59.60	1.59
7	0/34 (0.00)	11/54 (20.37)	7/58 (12.07)	18/146 (12.33)	55.00	6.78
8a	0/34 (0.00)	5/54 (9.26)	4/57 (7.02)	9/145 (6.21)	46.70	2.90
9	0/38 (0.00)	9/54 (16.67)	4/58 (6.9)	13/150 (8.67)	59.90	5.19
10	0/23 (0.00)	2/38 (5.26)	2/41 (4.88)	4/102 (3.92)	43.20	1.69
11p	0/34 (0.00)	6/48 (12.5)	6/49 (12.24)	12/131 (9.16)	64.80	5.94
11d	0/30 (0.00)	4/43 (9.3)	4/46 (8.7)	8/119 (6.72)	48.90	3.29
12a	0/29 (0.00)	0/37 (0.00)	2/49 (4.08)	2/115 (1.74)	0	0

TRG, tumor regression grade.

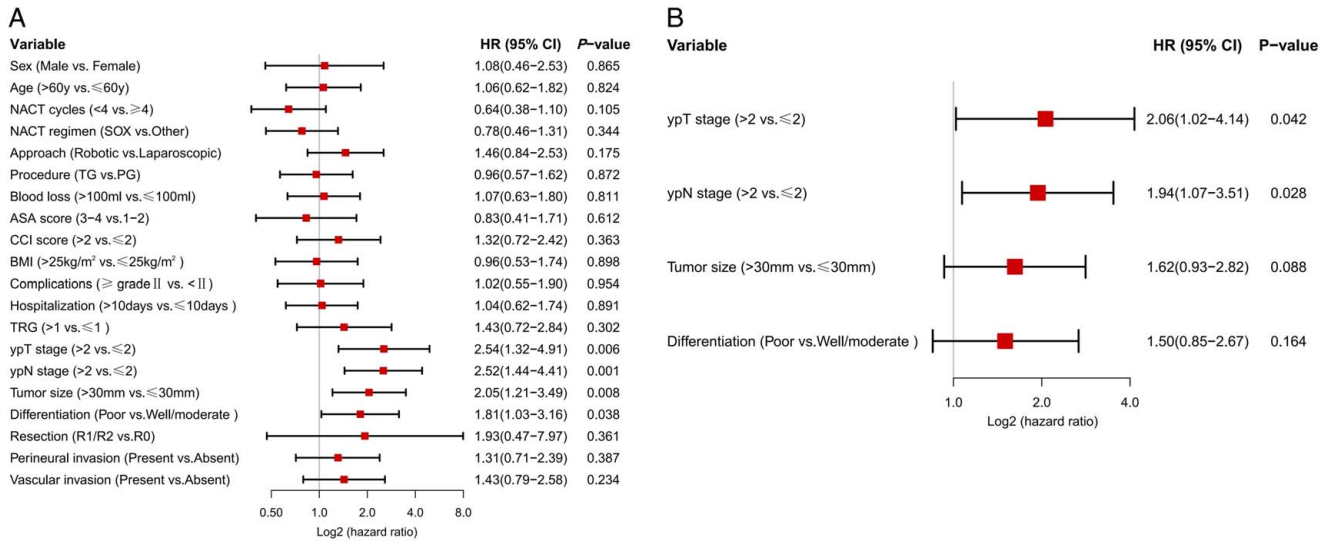

Figure 3. Forest plot of univariate (A) and multivariate (B) Cox regression analysis for overall survival. GC, gastric cancer; NACT, neoadjuvant chemotherapy; PG proximal gastrectomy; TG, total gastrectomy; TRG, tumor regression grade.

preservation merits prioritization for early proximal cancers where PG and TG have similar safety. This provides references for individualized treatment strategies.

Surgical concerns regarding the performance of PG in patients with upper GC primarily revolve around the inadequate lymph node dissection, consequently posing a risk of being unable to achieve an R0 resection[25]. However, investigating the lymph node metastasis rates in stations #4d, #5, #6, and #12a, which are dissected during TG but not in PG, can contribute to addressing this concern[23]. Previous studies in patient populations without NACT have already reported exceptionally low metastasis rates in these four lymph node groups. Yura *et al.*[17] reported a low lymph node metastasis rate in patients with T2/T3 proximal GCs, specifically at stations #4d, #5, #6, and #12a, with rates of 0.99%, 0, 0, and 0.006%, respectively. Sasako *et al.*[22]found the lowest therapeutic indices at stations #5 and #6 specifically for upper-third compared to middle- or lower-third tumors. Ooki *et al.*[26]also demonstrated 3.7, 2.4, and 0% nodal metastasis at #4d, #5, and #6 in T3 proximal cancers. Haruta *et al.*[27] further showed minimal metastasis rates of 3.3, 0.5, 1.6%, and 0% at stations #4d, #5, #6, and #12a, respectively, in proximal cancers. As described by Niihara *et al.*[28], in early proximal GC, the left gastric artery nodes (#1, #3, and #7) serve as primary drainage pathways, while the right gastric artery (#5, #8, and #12) and right gastroepiploic arteries (#4d and #6) represent distant regional routes rarely involved in initial metastasis. This elucidates the limited efficacy of prophylactic distal lymphadenectomy.

The present nodal dissection results align with previous studies, which demonstrated the limited therapeutic value of dissecting distal lymph node stations #4d, #5, #6, and #12a in proximal GC patients undergoing NACT followed by radical gastrectomy. Metastasis rates and indices at these stations were negligible, indicating proximal gastrectomy could achieve adequate lymphadenectomy without total gastrectomy in this population. Positivity rates at stations #4d, #5, #6, and #12a were notably low, with values of 2.74, 0.67, 1.33, and 1.74%, respectively, among TG patients. Moreover, the therapeutic value index for #4d, #5, #6, and #12a were 1.55, 2.33, 1.59, and 0, respectively, which significantly lower than other nodal stations. These findings suggest that proximal gastrectomy may offer an oncologically safe alternative to total gastrectomy for proximal cancers following NACT, particularly for TRG0/1 (#4d, #5, #6, and #12a: 0%, 0%, 0%, and 0%) and TRG2 (#4d, #5, #6, and #12a: 1.85%, 0%, 1.85%, and 0%) patients with even lower distal node positivity. With the advancement of deep learning radiomics nomograms, satisfactory discrimination of predicting TRG and the response to NACT before surgery in GC patients has been achieved[29]. Combining these techniques with our results could provide a more precise determination of the extent of lymph node dissection.

Limitations of this study include potential selection bias, as randomization was infeasible. Surgeons may have favored smaller tumors with wider margins for PG, influencing results. We also only evaluated oncological outcomes without considering patient quality of life. Furthermore, procedures may impact function differently, necessitating prospective research with patient-reported measures to fully compare trade-offs. The combination of NACT and immunotherapy was not investigated in the present study due to the limited number of cases.

Conclusion

In summary, this study provides qualified evidence to support oncologically safe PG preserving better function over TG for select proximal GC patients receiving NACT. But given study limitations, our findings warrant verification by high-quality research. We expect future large-scale multicenter prospective randomized trials to provide stronger clinical evidence guiding practice in this field.

Ethical approval

The study has been approved by the Ethics Committee of Chinese PLA General Hospital (No. S2023-370-01).

Consent

Informed consent was not required for this study.

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Author contribution

Z.Y.: data curation, conceptualization, writing – original draft preparation; H.C.: data curation, conceptualization, writing – reviewing and editing; Q.X.: methodology and software; J.G.: formal analysis and software; W.L.: conceptualization and methodology; B.C.: visualization and investigation; X.L.: data curation; L.S.: writing –reviewing and editing; J.H.: writing – reviewing and editing; R.Z.: methodology and software; H.L.: methodology and software; Z.Y.: methodology, software, and formal analysis; J.D.: methodology; S.W.: methodology; Y.Z.: conceptualization, data curation; L.C.: resources and supervision; J.C.: resources, funding acquisition, and supervision; B.W.: resources, funding acquisition, and supervision.

Conflicts of interest disclosures

The authors deny any conflict of interests.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

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Data availability statement

All original data are available upon reasonable request to the corresponding authors.

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This paper was not invited.

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