

Received: 2021.01.08

Accepted: 2021.04.24

Available online: 2021.05.25

Published: 2021.07.28

# Effects of Preoperative Pyloric Stenosis on Outcomes and Nutritional Status in 73 Patients Following Curative Gastrectomy for Gastric Cancer: A Retrospective Study from a Single Center

**Authors' Contribution:**

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

**CE 1 Xuguang Jiao**  
**BC 2 Yu Wang**  
**BF 3 Xiangyang Qu**  
**EG 1 Jianjun Qu**  
**AD 1 Xinbo Wang**

1 Department of Surgical Oncology, Weifang People's Hospital, Weifang, Shandong, PR China  
2 Department of Information Network Management, Weifang People's Hospital, Weifang, Shandong, PR China  
3 Department of Nephrology, Second People's Hospital of Weifang, Weifang, Shandong, PR China

**Corresponding Author:** Xinbo Wang, e-mail: [wfwangxb@126.com](mailto:wfwangxb@126.com)

**Source of support:** This study was supported by the Science and Technology Development Program of Weifang City (No. 2019YX002)

**Background:** The aim of this study was to explore the potential impact of pyloric stenosis (PS) on the nutritional status, the incidence of postoperative complications, and the long-term prognosis of distal gastric cancer (GC) patients after curative resection.


**Material/Methods:** We retrospectively analyzed the data of 343 GC patients who underwent curative gastrectomy for gastric cancer between January 2010 and December 2013. All patients were divided into 2 groups according to the status of PS. Their clinical and pathological features, nutritional indicators, and incidence of postoperative complications were compared and potential prognostic factors were analyzed using the propensity score matching analysis (PSM).

**Results:** Seventy-four (21.6%) patients had PS. Patients with PS had worse survival outcomes than those without PS ( $\chi^2=21.369$ ,  $P<0.001$ ). Multivariate survival analysis demonstrated that PS, depth of invasion, and lymph node metastasis (all  $P<0.05$ ) were the independent predictors of overall survival (OS). Patients with PS had significantly higher lymph node metastasis in No. 3, 4sb, 4d, 6, 8a, 9, and 14v lymph nodes. Patients with PS had significantly lower preoperative BMI, more weight loss, and lower prealbumin than those without PS. There were no significant differences between the 2 groups in postoperative complications, morbidity, or mortality.

**Conclusions:** Distal GC patients with PS have poor clinicopathological and nutritional status and poor prognosis. However, PS does not increase surgery-related morbidity and mortality.

**Keywords:** **Postoperative Complications • Prognosis • Pyloric Stenosis • Stomach Neoplasms**

**Full-text PDF:** <https://www.medscimonit.com/abstract/index/idArt/930974>

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## Background

Although epidemiology shows that the incidence of fundus and cardia gastric cancer has increased significantly in recent years, the most common site of GC is still in the distal third part [1-3]. With the improvement of surgical technique and adjuvant treatment level, the prognosis of GC patients has been improved, but it is still unsatisfactory. T stage, N stage, intraoperative blood loss, and other intraoperative and postoperative indicators have been confirmed to be related to the prognosis of GC patients [4-6]. In addition to these factors, some potential preoperative indicators related to the prognosis of gastric cancer have been reported in recent years, such as pyloric stenosis (PS) [7,8].

The pylorus connects the stomach and the duodenum. Tumors growing in the antrum of the stomach tend to invade the pylorus, inducing a mechanical impediment to gastric emptying, which in turn leads to PS [9,10]. Therefore, PS is one of the common complications in patients with distal GC. In China, many GC patients present with advanced disease at the time of diagnosis due to lack of an effective GC screening system and medical common sense, resulting in a high proportion of patients with PS, especially in rural areas.

Patients with PS usually present with abdominal distension, vomiting, and other obstructive symptoms. Chyme cannot reach the small intestine fully through the pylorus, resulting in digestive and absorptive disorders. In addition, the accumulation of food causes hyperdistention of the stomach, thus leading to edema of the gastric wall. Therefore, it is speculated that surgery is associated with a relatively high complication morbidity and mortality due to the poor nutrition and general status or progressing tumor infiltration in these patients.

Wu et al [8] demonstrated that distal GC patients with PS have worse biological behavior than those without PS, consequently leading to poor prognosis. Unfortunately, nutritional status of patients and the incidence of postoperative complications were not further analyzed in their study. Therefore, we investigated the potential impact of PS on nutritional status, postoperative complications and prognosis of distal GC after curative resection.

## Material and Methods

### Patients and Data

We reviewed and analyzed data from 343 distal GC patients between January 2010 and December 2013 at the Department of Surgical Oncology, Weifang People's Hospital. All patients underwent radical gastrectomy and lymph node dissection.

The eligibility criteria included: 1) pathologically confirmed adenocarcinoma; 2) the lesion was located in the distal third part of the stomach; 3) patients received radical gastrectomy (R0) with D1 or D2 lymphadenectomy; 4) more than 15 dissected lymph nodes; 5) no history of neoadjuvant chemotherapy.

The exclusion criteria included: 1) fundus and cardia gastric cancer; 2) patients with distant metastasis; 3) patients lost to follow-up.

All patients were divided into 2 groups according to the status of PS. PS was defined as when a conventional endoscope could not be passed to the duodenum or patients had obstructive symptoms, such as upper abdominal distension, nausea, and vomiting. The independent Ethics Committee of Weifang People's Hospital (Shandong, China) approved this study.

### Surgical Procedures and Perioperative Care

Radical gastrectomy and systematic lymph node dissection were performed for all patients. The reconstruction method of digestive tract was determined by the surgeon according to the intraoperative situation. Patients with PS were treated with continuous gastrointestinal decompression and intensive gastric cavity lavage using concentrated sodium chloride solution for 3 to 5 days. At the same time, intravenous nutritional support was performed before the operation. After surgery, intravenous nutrition was used until the patient had flatus, and then started eating a fluid diet.

### Clinicopathological Data and Survival

The patients' demographic data included sex, age, gastrectomy, tumor size, type of reconstruction, Lauren's classification, T stage, N stage, adjuvant chemotherapy, number of examined lymph nodes, number of positive lymph nodes, and No. 1 to No. 14v lymph node metastasis. We first compared the clinicopathological parameters between the 2 groups using the propensity score analysis. Survival analysis was then performed to identify risk factors that affected the patient's prognosis. We next compared the nutritional indicator differences between the 2 groups. Finally, the postoperative complications morbidity and mortality were compared and summarized. Tumor staging was conducted according to the seventh edition of the UICC TNM classification system. Lymph node dissection was performed in accordance with Japanese gastric cancer treatment guidelines 2018 (5<sup>th</sup> edition) [11].

### Follow-Up

For the initial 2 years following gastrectomy, the patients had follow-up once every 3 months. Then, at 2-5 years following gastrectomy, the patients underwent follow-up once every 6

months. After 5 years, annual patient follow-up was undertaken. The results of each review were recorded in detail.

### Statistical Analysis

Categorical variables were compared using the chi-square test, and *t* tests were used for comparing continuous variables. Overall survival (OS) and disease-free survival (DFS) were evaluated using the Kaplan-Meier method, and statistical differences between groups were evaluated using the log-rank test. Prognostic factors were evaluated by Cox regression model.

A propensity score analysis was performed to overcome bias due to the different distribution of covariates among patients with PS and those without PS. Variables entered in the propensity model were sex, age at surgery, tumor size, type of gastrectomy, type of reconstruction, Lauren's classification, adjuvant chemotherapy, depth of invasion, and lymph node metastasis. Nearest neighbor matching was performed in a 1:1 ratio without replacement, and a caliper width with a 0.01 standard deviation was specified. For all analyses,  $P < 0.05$  was considered statistically significant. All statistical analyses were performed using SPSS software version 24.0 (SPSS, Inc, Chicago, IL USA).

## Results

### Patient Characteristics

Among all the 343 patients with distal GC, 74 patients (21.6%) had PS. The size of tumors in patients with PS was larger than that in patients without PS ( $5.196 \pm 2.142$  vs  $4.555 \pm 2.456$ ,  $t = 2.042$   $P = 0.042$ ). Patients in the PS group had a higher total gastrectomy rate than those in the non-PS group (16.2% vs 7.4%,  $\chi^2 = 5.290$   $P = 0.039$ ). The proportion of Billroth II and Roux-en-Y reconstruction in the PS group was larger than that in the non-PS group (35.1% vs 27.2%, 16.2% vs 7.5%). However, the proportion of Billroth I reconstruction in patients with PS was lower (48.6% vs 65.3%). Patients with PS had deeper tumor invasion, more lymph node metastasis, more examined lymph nodes ( $t = 2.077$   $P = 0.039$ ), and more positive lymph nodes ( $t = 5.171$   $P < 0.001$ ) than patients without PS (Table 1).

### PSM Analysis

After a 1:1 matching according to the propensity score, 74 patients without PS were matched to 74 patients with PS. The basic covariates between the 2 groups in the matched data are listed in Table 1. After matching, all of the baseline characteristics became comparable between the 2 groups, except for N stage.

### Survival Analysis

The 5-year OS rate of patients with PS and without PS were 20.4 and 51.2%, respectively ( $P < 0.001$ ) (Figure 1), and the 5-year DFS rates of patients with PS and without PS were 25.8 and 55.6%, respectively ( $P < 0.001$ ) (Figure 2) in the whole study. After matching, the 5-year OS rate of patients with PS and without PS were 20.4% and 50.8%, respectively ( $P = 0.007$ ) (Figure 3), and the 5-year DFS rates of patients with PS and without PS were 25.8% and 51.3%, respectively ( $P = 0.006$ ) (Figure 4) in the propensity-matched cohort.

The results of survival analysis are shown in Tables 2 and 3. Univariate analysis showed that tumor size, type of reconstruction, PS, depth of tumor invasion, and lymph node metastasis were associated with prognosis of all distal GC patients in the whole study. After matching, PS, depth of tumor invasion, and lymph node metastasis were associated with prognosis of all distal GC patients (Table 2). Multivariate analysis revealed that PS, depth of invasion, and lymph node metastasis were independent prognostic factors for distal GC patients, both in the whole study and in propensity score-matched pairs (Table 3).

### Lymph Node Metastasis

The lymph node metastasis of patients in the 2 groups after matching are shown in Table 4. Patients with PS had significantly higher lymph node metastasis in No. 3, 4sb, 4d, 6, 8a, 9, and 14v lymph nodes, while there were no differences in lymph node metastasis in No. 1, 2, 4sa, 5, 7, 10, 11p, 11d, 12a, and 13 lymph nodes.

### Nutritional Factors and Postoperative Complications

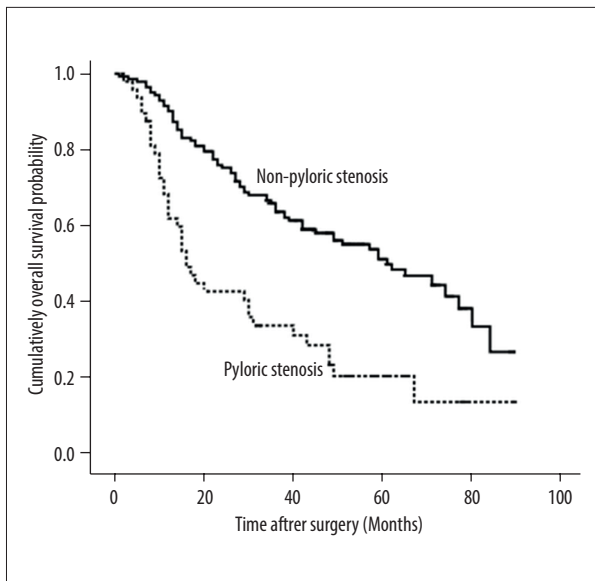
Table 5 shows the comparison of the main nutritional indexes between the 2 groups. Compared with patients without PS, body weight loss and body mass index (BMI) were significantly reduced, but the mid-arm circumference (MAC), hemoglobin, albumin, prealbumin, transferrin, total protein, total cholesterol, and total lymphocyte count (TLC) did not decrease before the operation in patients with PS. Table 6 shows the comparison of postoperative complications morbidity and mortality between the 2 groups. There were no differences in postoperative complications morbidity and mortality between patients with and without PS.

## Discussion

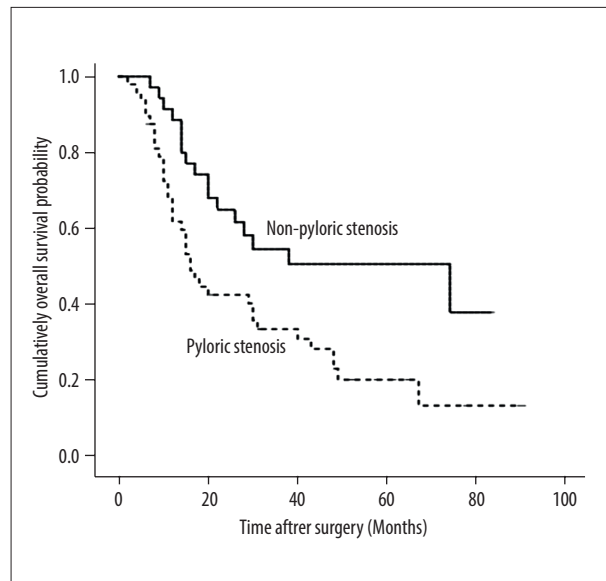
PS is a series of complications from any disease that progresses to mechanical obstruction of gastric emptying. It can be caused by tumors from the stomach and pancreas, congenital diseases, obstruction from acute edema, chronic scarring

**Table 1.** Comparison of clinicopathologic characteristics between patients with and without pyloric stenosis.

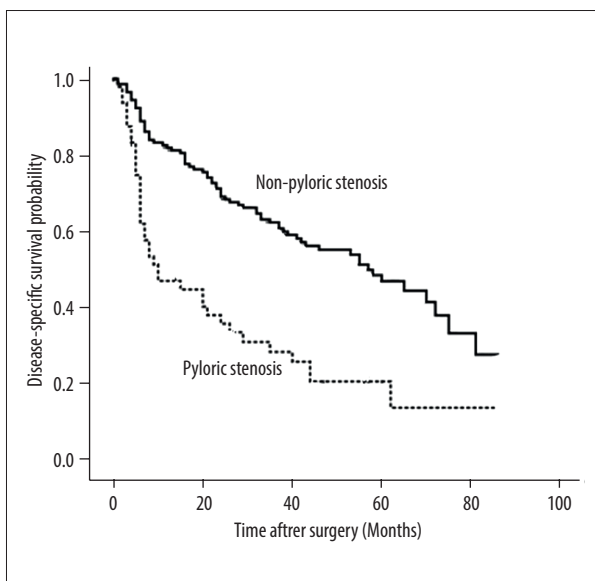
Variables	Whole study series			Propensity-score-matched pairs	
	Pyloric stenosis 74 cases (%)	Non-pyloric stenosis 269 cases (%)	<i>P</i>	Non-pyloric stenosis 74 cases (%)	<i>P</i>
Gender			0.135		0.721
Male	53 (71.6)	167 (62.1)		50 (67.7)	
Female	21 (28.4)	102 (37.9)		24 (32.4)	
Age at surgery (years)	59.01±11.057	57.36±11.252	0.262	57.00±10.347	0.255
Tumor size (cm)	65.196±2.142	4.555±2.456	<b>0.042</b>	5.457±2.824	0.528
Type of gastrectomy			<b>0.039</b>		0.818
Distal	62 (83.8)	249 (92.6)		64 (86.5)	
Total	12 (16.2)	20 (7.4)		10 (13.5)	
Type of reconstruction			<b>0.014</b>		0.889
Billroth I	36 (48.6)	175 (65.3)		38 (51.4)	
Billroth II	26 (35.1)	73 (27.2)		26 (35.1)	
Roux-en Y	12 (16.2)	20 (7.5)		10 (10.0)	
Lauren's classification			0.067		0.471
Intestinal	12 (16.2)	73 (27.1)		8 (10.8)	
Diffuse	62 (83.8)	196 (72.9)		66 (89.2)	
Depth of invasion			<b>0.001</b>		0.879
T1	0 (0)	11 (4.1)		0	
T2	0 (0)	26 (9.7)		0	
T3	3 (4.1)	34 (12.6)		2 (2.7)	
T4a	63 (85.1)	185 (68.8)		63 (85.1)	
T4b	8 (10.8)	13 (4.8)		9 (12.2)	
Lymph node metastasis			<b>&lt;0.001</b>		<b>0.028</b>
N0	5 (6.8)	117 (43.5)		0	
N1	16 (21.6)	28 (10.4)		19 (25.7)	
N2	11 (14.9)	54 (20.1)		3 (4.1)	
N3a	30 (40.5)	53 (19.7)		37 (50)	
N3b	12 (16.2)	17 (6.3)		15 (20.3)	
Adjuvant chemotherapy			0.492		1
No	23 (31.1)	97 (36.1)		23 (31.1)	
Yes	51 (68.9)	172 (63.9)		51 (68.9)	
Number of examined lymph nodes	25.36±9.47	22.82±8.60	<b>0.039</b>	27.51±11.24	0.208
Number of positive lymph nodes	8.69±7.94	4.33±5.95	<b>&lt;0.001</b>	9.97±7.23	0.306



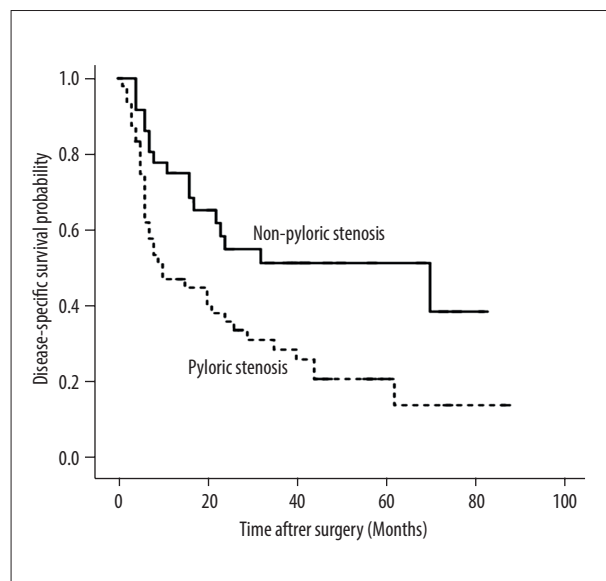
**Figure 1.** Overall survival curves for all patients with or without pyloric stenosis. ( $p < 0.001$ )



**Figure 3.** Overall survival curves for patients with or without pyloric stenosis in the propensity score-matched cohort. ( $P = 0.007$ )



**Figure 2.** Disease-free survival curves for all patients with or without pyloric stenosis ( $P < 0.001$ ).



**Figure 4.** Disease-free survival curves for all patients with or without pyloric stenosis in the propensity score-matched cohort ( $P = 0.006$ ).

and fibrosis, or a combination of these [12-15]. Among them, GC is the most common malignant cause of PS. It has been reported that 15-30% of distal GC patients were accompanied by different degrees of PS at the time of initial diagnosis [9,15]. In our study, 21.6% of distal GC patients suffered from PS. Compared with all reported studies, the proportion of patients was higher because most of the patients with GC in this study came from rural areas of China. PS has been reported to be more prevalent in people with low socio-economic status, and our results are similar to other findings [16,17].

Chen et al [8] reported that tumor size was larger in patients with PS than in those without PS. In this study, we found that the incidence of PS increased significantly when the tumor diameter of distal GC was larger than 5 cm. When the tumor is too large to ensure that the upper margin of distal gastrectomy is negative, total gastrectomy is often performed. The tumor invades the pylorus, adjacent to the duodenum, often leading to duodenal bulbar edema, so the proportion of B-I gastrointestinal reconstruction is lower than that of patients without obstruction.

**Table 2.** Univariate survival analysis of all gastric cancer patients in the whole study series and propensity score-matched pairs.

Variables	Whole study series			Propensity-score-matched pairs		
	5YSR	$\chi^2$	<i>p</i>	5YSR	$\chi^2$	<i>p</i>
Gender		0.911	0.340		0.377	0.539
Male	41.0			20.8		
Female	47.5			29.6		
Age at surgery (year)		2.762	0.097		0.548	0.459
<60	46.0			34.0		
≥60	38.0			26.7		
Tumor size (cm)		12.182	<0.001		0.859	0.354
<5	52.5			28.0		
≥5	32.5			19.1		
Type of gastrectomy		1.297	0.255		0.080	0.777
Distal	43.7			34.6		
Total	36.4			22.9		
Type of reconstruction		7.688	0.021		2.955	0.228
Billroth I	50.2			37.4		
Billroth II	29.7			26.2		
Roux-en Y	36.4			22.9		
Lauren's classification		0.024	0.878		0.376	0.540
Intestinal	46.9			32.9		
Diffuse	42.3			25.6		
Adjuvant chemotherapy		2.700	0.100		0.325	0.569
No	33.6			26.8		
Yes	42.8			33.3		
Pyloric stenosis		21.369	<0.001		7.167	0.007
No	51.2			38.1		
Yes	20.4			20.4		
Depth of invasion		22.145	<0.001		17.014	<0.001
T1	87.5			–		
T2	64.9			–		
T3	55.4			33.3		
T4a	37.3			36.1		
T4b	18.2			11.1		
Lymph node metastasis		64.107	<0.001		11.955	0.018
N0	69.9			50.0		
N1	64.2			56.5		
N2	30.1			34.1		
N3a	16.5			19.8		
N3b	7.1			19.2		



**Table 3.** Multivariate survival analysis of all gastric cancer patients in the whole study series and propensity score-matched pairs.

Variables	Whole study series		Propensity-score-matched pairs	
	HR (95% CI)	p	HR (95% CI)	p
Pyloric stenosis		<b>0.025</b>		<b>0.002</b>
No	1		1	
Yes	1.658 (1.066-2.580)		2.595 (1.408-4.783)	
Depth of invasion		<b>0.021</b>		<b>0.001</b>
T1	1		–	
T2	0.729 (0.199-2.669)	0.633	–	
T3	1.562 (0.520-4.692)	0.427	1	
T4a	0.902 (0.320-2.544)	0.846	0.197 (0.049-0.787)	0.805
T4b	2.830 (0.836-9.580)	0.095	1.830 (0.174-3.881)	<b>0.021</b>
Lymph node metastasis		<b>&lt;0.001</b>		<b>0.005</b>
N0	1		1	
N1	1.355 (0.559-3.285)	0.502	0.572 (0.135-2.421)	0.448
N2	2.763 (1.434-5.323)	<b>0.002</b>	0.937 (0.218-4.029)	0.931
N3a	4.736 (2.540-8.829)	<b>&lt;0.001</b>	2.695 (0.691-10.507)	0.153
N3b	7.679 (3.427-17.207)	<b>&lt;0.001</b>	3.183 (0.745-13.594)	0.118

In our study, distal gastric cancer patients with PS had poorer 5-year OS rate and DFS rate than in those without PS both in the whole study and in the propensity-matched cohort. Chen et al [8] reported that most of the GC patients with PS were in advanced stages. Although radical resection was performed, their 5-year OS was only 42.8%, while the postoperative 5-year OS was up to 78.6% in patients without PS. Similar to Chen's findings, Huang's study showed that the 5-year OS was 38.8% in patients with PS and 62.4% in those without PS. GC patients with PS not only have low survival rate but also low surgical resection rate. Watanabe et al [18] reported that 22% of GC patients with PS underwent non-curative resection or no resection, and the 5-year OS rate of those patients was 22%, which was lower than 58% in the non-PS group. In our study, the 5-year OS rate of the patients with PS was 20.4%, which was lower than the 51.2% in patients without PS. Our data are in accordance with Chen and Huang's reports.

Late pathological stage is one of the main causes for poor prognosis in PS patients. We noted that patients with PS had deeper cancer invasion and more lymph node metastasis than those without PS. All patients in the PS group had more serosal invasion. In addition, the larger diameter of the tumor leads to high tumor burden in the patients with PS. Unfortunately, depth of tumor invasion and tumor size are 2 recognized prognostic factors associated with poor prognosis in GC patients [19-21].

It has been confirmed that the lymph node involvement is related to the prognosis in GC after curative gastrectomy. Patients with positive lymph nodes usually have poorer survival than those with node-negative disease [22]. In our study, 93.2% of the patients with PS had positive lymph node metastasis and patients with PS had more examined lymph nodes and positive lymph nodes than those without PS. This could be the result of deeper tumor invasion and larger tumor size. Furthermore, Chen et al [8] noticed that patients with PS had a high incidence of lymph node metastasis to the hepatoduodenal ligament and retropancreatic regions. Lymph node metastasis in these regions predicts a poor prognosis. In the present study, patients with PS were more likely to have lymph node metastasis to No. 3, 4sb, 4d, 6, 8a, 9, and 14v lymph node stations. This may be because these lymph nodes are anatomically closer to the pylorus.

Whether PS can affect the safety of radical gastrectomy is still controversial. Bozzetti et al [23] reported that GC patients with PS were prone to malnutrition such as hypoalbuminemia and weight loss before the operation, resulting in an increase in the incidence of postoperative complications. However, the study by Park et al [24] found that there were no statistically significant differences in postoperative complications that required physicians' intervention between patients with PS and those without PS. In the current study, the incidences of postoperative complications and mortality were 12.2% and 5.9% vs

**Table 4.** Lymph node metastasis status in the propensity score-matched pairs.

Lymph node	Pyloric stenosis +%	Non-pyloric stenosis +%	$\chi^2$	<i>p</i>
No.1	32.3	25.3	0.174	0.126
No.2	44.4	21.8	0.296	0.201
No.3	72.6	39.8	21.245	<b>&lt;0.001</b>
No.4sa	0	1.9	1.401	0.589
No.4sb	57.1	20.1	6.877	<b>0.019</b>
No.4d	48.8	23.1	8.165	<b>0.007</b>
No.5	18.9	24.3	0.638	0.550
No.6	51.4	29.9	12.958	<b>&lt;0.001</b>
No.7	30.0	20.3	3.546	0.079
No.8a	43.8	22.3	7.531	<b>0.010</b>
No.9	33.3	12.3	6.915	<b>0.029</b>
No.10	66.7	20.1	2.222	0.400
No.11p	75.0	22.2	3.259	0.071
No.11d	0	50.0	1.875	0.400
No.12a	9.5	8.6	0.060	0.817
No.13	2.7	5.4	0.695	0.681
No.14v	5.4	0.4	10.237	<b>0.008</b>

**Table 5.** Anthropometric and laboratory data according to nutritional status in the propensity score-matched pairs (mean±SD).

Parameters	Pyloric stenosis	Non-pyloric stenosis	<i>t</i>	<i>p</i>
Weight (kg)	62.00±12.34	63.01±9.83	0.931	0.368
Weight loss (kg)	6.52±4.29	4.51±2.76	2.722	<b>0.010</b>
BMI (kg/m <sup>2</sup> )	22.50±3.03	25.54±2.61	2.300	<b>0.041</b>
MAC (cm)	28.80±3.60	29.710±3.290	0.997	0.313
Hemoglobin (g/L)	125.51±22.31	127.35±26.81	0.293	0.799
Albumin (g/L)	40.36±5.18	42.86±23.54	0.899	0.369
Prealbumin (g/L)	268.30±51.30	283.21±54.08	<b>2.920</b>	<b>0.009</b>
Transferrin (g/L)	2.40±0.20	2.430±0.18	1.631	0.114
Total protein (g/L)	68.16±10.95	70.51±9.01	1.781	0.098
Total cholesterol (mg/dL)	167.973±10.779	172.179±9.194	1.503	0.151
TLC (×10 <sup>9</sup> /L)	0.29±0.10	0.31±0.12	1.730	0.109

All *P* values were determined with the use of independent *t* test. BMI – body mass index; MAC – midarm circumference; TLC – total lymphocyte count.



**Table 6.** Comparison of postoperative complications morbidity and mortality between the 2 groups.

Parameters	Pyloric stenosis 74 cases	Non-pyloric stenosis 269 cases	$\chi^2$	<i>p</i>
Overall complications	9	16	3.317	0.079
Major surgical complications	6	10	2.516	0.124
Stomach empty postpone	2	3	1.018	0.295
Ileus	1	3	0.028	0.867
Intra-abdominal infection	1	3	0.028	0.867
Anastomotic leak	2	1	3.637	0.057
Non-surgical complication	3	6	0.755	0.412
Pneumonia	1	2	0.247	0.519
Cardiovascular disorders	1	1	0.961	0.385
Urinary system infection	0	1	0.276	0.784
Hepatic impairment	1	2	0.247	0.519
In-hospital mortality	0	1	0.276	0.784

0% and 0.3%, respectively, in the PS group and non-PS group. There were no statistically significant differences in morbidity and mortality. By analyzing the main nutritional indicators of the 2 groups of patients, we found patients with PS had significantly lower preoperative BMI, more weight loss, and lower serum prealbumin content than those without PS. However, the differences in these 3 nutritional indicators did not affect the significant differences in postoperative incidence of complications and mortality. This may be related to our preoperative nutritional support and gastrointestinal preparation for patients with PS.

There are several limitations to our study. First, although a PSM analysis was performed to avoid biases in the selection of the patients, this was a single-institution, retrospective study with a small sample size. Second, due to disorders of digestion and absorption, the proportion of patients with PS receiving neoadjuvant chemotherapy was very small, so this group of patients was not included in this study. Third, postoperative nutritional indicators were not compared between the 2 groups.

## Conclusions

In conclusion, distal gastric cancer patients with PS are at more advanced stages and have poor nutritional status, resulting in poor prognosis. Nevertheless, the incidence of postoperative complications and mortality did not increase significantly after adequate nutritional support and gastrointestinal preparation before the operation. Therefore, it is very important to strengthen nutrition management in the preoperative period and postoperative follow-up, and adjuvant therapy such as chemotherapy should be considered in distal GC patients with PS.

## Conflict of Interest

None.

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