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### Presentation

This research won the Best Oral Presentation Award at the KINGCA week 2022. The study Comparing Pre- and Post-Operative Findings in Patients Who Underwent Laparoscopic Proximal Gastrectomy With a Double-Flap Technique: A Study on High-Resolution Manometry, Impedance pH Monitoring, and Esophagogastroduodenoscopy Findings

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# ABSTRACT

**Purpose:** Laparoscopic proximal gastrectomy (LPG) is a viable choice for treating proximal gastric lesions. However, the occurrence of severe reflux has limited its widespread adoption. To address this issue, the double flap technique (DFT), which incorporates artificial lower esophageal sphincteroplasty, has been developed to prevent reflux problems after proximal gastrectomy. In this study, we aimed to investigate the usefulness of this technique using high-resolution manometry (HRM), impedance pH monitoring, and esophagogastroduodenoscopy (EGD).

**Materials and Methods:** The findings of pre- and postoperative 6-month HRM, pH monitoring, and EGD were compared for 9 patients who underwent LPG with DFT for various proximal gastric lesions at Incheon St. Mary's Hospital from January 2021 to December. **Results:** A total of 9 patients underwent proximal gastrectomy. Approximately half of the patients had Hill's grade under II preoperatively, whereas all patients had Hill's grades I and II in EGD findings. In the HRM test, there was no significant difference between distal contractile integral (1,412.46±1,168.51 vs. 852.66±495.62 mmHg·cm·s, P=0.087) and integrated relaxation pressure (12.54±8.97 vs. 8.33±11.30 mmHg, P=0.27). The average lower esophageal sphincter (LES) pressure was 29.19±14.51 mmHg preoperatively, which did not differ from 19.97±18.03 mmHg after the surgery (P=0.17). DeMeester score (7.02±6.36 vs. 21.92±36.17, P=0.21) and total acid exposure time (1.49±1.48 vs. 5.61±10.17, P=0.24) were slightly higher, but the differences were not statistically significant.

**Conclusions:** There is no significant functional difference in HRM and impedance pH monitoring tests after DFT. DFT appears to be useful in preserving LES function following proximal gastrectomy.

**Keywords:** Gastrectomy; Gastroesophageal reflux; Lower esophageal sphincter; Ambulatory 24-hour esophageal pH monitoring; Manometry



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#### **Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

#### **Author Contributions**

Conceptualization: K.J.J.; Data curation: Y.H.J.; Formal analysis: Y.H.J.; Investigation: Y.H.J., K.J.J.; Methodology: Y.H.J., K.J.J.; Project administration: K.J.J.; Supervision: K.J.J.; Validation: K.J.J.; Visualization: Y.H.J.; Writing - original draft: Y.H.J.; Writing - review & editing: Y.H.J., K.J.J.

## **INTRODUCTION**

Gastric cancer is the 5th most frequently diagnosed cancer worldwide. In South Korea, the age-standardized incidence rate of gastric cancer is 40 per 100,000 person-years, which is 8 times higher than in North America and Europe [1,2]. The majority of the South Korean population previously had distal gastric cancer [1,3]. However, there has been a change in this trend in recent years, with a continuous increase in the incidence of lesions in the gastroesophageal junction (GEJ) and the upper 1/3 of the stomach [1,4,5]. For lesions involving the GEJ and upper 1/3 of the stomach, 2 options are considered: total gastrectomy and proximal gastrectomy. Traditionally, many surgeons perform total gastrectomies. However, there is a high rate of postoperative complications and morbidity, which is a major concern. These complications include postoperative reflux esophagitis and anastomotic stenosis, which can negatively impact the quality of life for patients. Furthermore, longterm malnutrition is another serious problem [6-8]. From this perspective, proximal gastrectomy not only has the advantage of a lower occurrence of postoperative complications, but also offers functional preservation [8,9]. Additionally, several studies have reported relatively shorter operation times, improved postoperative nutritional status, and a lower incidence of dumping syndrome [9-12]. A recent meta-analysis also demonstrated that patients who underwent proximal gastrectomy experienced a lower prevalence of anemia and body weight loss compared to those who underwent total gastrectomy [8]. Although proximal gastrectomy is likely to have good functional outcomes, the question that needs to be addressed is postoperative reflux esophagitis when simple esophagogastrostomy is performed [12,13]. To prevent reflux esophagitis, various anastomosis techniques have been proposed, such as jejunal interposition and jejunal pouch formation [7,14,15]. Conversely, the double flap technique (DFT) focuses on creating an artificial flap valve directly at the anastomosis. DFT was first introduced in the mid-1990s and allows for the functional preservation of the GEJ with an artificial sphincteroplasty [16]. This method has been considered a viable alternative to other esophagogastrostomies, but there have been few studies examining postoperative functional evaluation. Due to this lack of research, we aim to investigate the functional outcomes of DFT by comparing pre- and postoperative EGD, high-resolution manometry (HRM), and impedance pH monitoring.

# **MATERIALS AND METHODS**

### Patients

The medical records of patients who underwent laparoscopic proximal gastrectomy (LPG) with DFT at Incheon St. Mary's Hospital from January 2021 to December 2021 for proximal gastric lesions were retrospectively reviewed. We included patients with malignancies and benign neoplasms located in the GEJ and upper 1/3 of the stomach. Patients with clinical stage IV, non-curative resection, and incomplete records were excluded. This study included the remaining 9 patients.

### **Operative procedure**

After the resection, the distal remnant stomach was removed from the abdomen through an umbilical port site. An extracorporeal double flap was constructed, with the flap's width measuring 2.5 cm and its length measuring 3.5 cm. The top side of the flap was positioned 2 cm distal to the proximal resection line of the remnant stomach, and a 2-cm hole was made on its bottom side for an esophagogastrostomy. Subsequent anastomosis procedures were



performed intracorporeally. Initially, stay sutures were placed between the top side of the flap and the posterior wall of the esophagus, 5 cm proximal to the resection line. Once the staple line on the distal esophagus was removed, a hand-sewn esophagogastrostomy was conducted using interrupted sutures or a continuous running suture with a barbed suture. The final step of this anastomosis involved suturing the flap onto the esophagogastrostomy.

### **Data collection**

From the review of medical records, we collected basic demographic information on preoperative patients, including sex, age, diagnosis, and American Society of Anesthesiologists classification. At our center, we routinely conducted endoscopy, HRM (using ManoScan<sup>™</sup> by Medtronic, Minneapolis, MN, USA), and impedance pH monitoring (using Digitrapper<sup>™</sup> by Medtronic) both before and 6 months after surgery to assess the functional status of these patients. In the endoscopic assessment, the degree of reflux esophagitis was described using the Los Angeles classification [17]. We evaluated the presence and grade of hiatal hernia using Hill's grade [18]. Regarding the HRM metrics, we measured various key values including distal contractile integral (DCI), integrated relaxation pressure (IRP), distal latency (DL), and lower esophageal sphincter (LES) pressure, according to the definition provided by Chicago Classification version 3.0 [19]. Using impedance pH monitoring, we counted the acid exposure time (AET) and the total number of refluxes. The DeMeester score (DMS) was automatically calculated using the designated protocol [20].

### **Statistical analyses**

The comparison between the pre- and postoperative functional findings in the pilot groups was evaluated using the Mann-Whitney U test for continuous variables, the  $\chi^2$  test, and Fisher's exact test for nominal variables. A P-value less than 0.05 is considered statistically significant. All statistical analyses were conducted using the software package STATA 17 for Windows (StataCorp LLC, College Station, TX, USA). The study was approved by the Institutional Review Board (IRB) of Incheon St. Mary's Hospital, The Catholic University of Korea (IRB number: OC23RASI0018).

# RESULTS

Nine patients underwent LPG with DFT in the year 2021. The average age was about 62.44 years old. Five patients had non-GEJ cancer, and 2 patients were diagnosed with GEJ cancer. Additionally, patients with gastrointestinal stromal tumor and leiomyoma were included (**Table 1**).

Two out of 9 patients underwent an endoscopic ballooning procedure to treat anastomotic stenosis. One patient had a single session, while the other had 3 sessions. Since endoscopic ballooning could negatively affect the flap valve function, the analyses were performed separately for the patients without (Group A) and with (Group B) ballooning (**Table 2**). Both groups had postoperative Hill's grade below II. Group A showed a statistically significant difference in Hill's grade after surgery with a P-value of 0.0167. However, this difference was not observed in Group B (P=0.06). Both groups had minimal or normal findings for reflux esophagitis.

**Table 3** displays the HRM results, which indicate that there was no significant difference in HRM metrics, such as DCI, IRP, and DL, between both groups. The average LES pressure after surgery was 22.24±19.93 mmHg in Group A and 19.97±18.03 mmHg in Group B, with



Table 1. Basic patient demographics

Table II basic patient demographies	
Categories	Value
Age (yr)	62.44±11.65
Sex	
Male	5 (55.56)
Female	4 (44.44)
Height (cm)	162.09±10.80
Body weight (kg)	68.12±13.37
BMI (kg/m²)	25.90±3.83
ASA classification	
1	1 (11.11)
2	7 (77.78)
3	1 (11.11)
4	0 (0)
5	0 (0)
Comorbidity	
Yes	8 (88.89)
No	1 (11.11)
Disease	
Non-GEJ gastric cancer	5 (55.56)
GEJ cancer	2 (22.22)
GIST	1 (11.11)
Others	1 (11.11)
Preoperative Sx	
Yes	5 (55.56)
No	4 (44.44)
PPI usage	
Yes	0 (0)
No	9 (100)

Values are presented as mean ± standard deviation or number (%).

BMI = body mass index; ASA = American Society of Anesthesiologists; GEJ = gastroesophageal junction; GIST = gastrointestinal stromal tumor; Sx = symptom; PPI = proton pump inhibitor.

all average LES pressures falling within the reference range. In the results of the 24-hour pH monitoring (as shown in **Table 4**), there was no statistical difference in DMS, AET, and the number of refluxes after surgery. However, when the patients who received postoperative ballooning were included, DMS increased up to 21. There were 2 cases diagnosed with GEJ cancer. **Fig. 1** displays the HRM result for one of the patients with GEJ cancer. In this

### Table 2. Pre- and post-esophagogastroduodenoscopy findings

Variables	Group A* (n=7)			Group B <sup>†</sup> (n=9)			
	Preoperative	Postoperative	P-value	Preoperative	Postoperative	P-value	
Hiatal hernia (Hill's grade)			0.017‡			0.060	
I. I.	2 (28.57)	4 (57.14)		2 (22.22)	6 (66.67)		
П	1 (14.29)	3 (42.86)		3 (33.33)	3 (33.33)		
III	4 (57.14)	0 (0)		4 (44.44)	0 (0)		
IV	0 (0)	0 (0)		0 (0)	0 (0)		
Reflux esophagitis			0.356	5 (55.56)	7 (77.78)	0.860	
Normal	4 (57.14)	6 (85.71)		4 (44.44)	2 (22.22)		
Minimal	3 (42.86)	1 (14.29)					
LA-A	0 (0)	0 (0)		0 (0)	0 (0)		
LA-B	0 (0)	0 (0)		0 (0)	0 (0)		
LA-C	0 (0)	0 (0)		0 (0)	0 (0)		
LA-D	0 (0)	0 (0)		0 (0)	0 (0)		

Values are presented as number (%).

\*Patient group excluding ballooning procedure.

<sup>†</sup>Patient group including ballooning procedure.

<sup>‡</sup>P<0.05.

LA = Los Angeles classification.



#### Table 3. Pre- and postoperative high-resolution manometry

Variables	Group A* (n=7)			Group B <sup>†</sup> (n=9)		
	Preoperative	Postoperative	P-value	Preoperative	Postoperative	P-value
DCI (mmHg·cm·s)	951.47±589.40	$712.69 \pm 257.56$	0.360	$1,412.46 \pm 1,168.51$	852.66±495.62	0.087
IRP (mmHg)	10.77±9.19	10.26±13.49	0.880	12.54±8.97	8.33±12.30	0.270
Median IRP ≥15 mmHg	1 (14.29)	2 (28.57)		1 (11.11)	2 (22.22)	
DL (sec)	6.83±0.75	6.77±1.43	0.920	6.72±0.77	6.72±1.29	1.000
LES pressure (mmHg)	25.94±13.95	22.24±19.93	0.580	29.19±13.70	19.97±18.03	0.170

Values are presented as mean ± standard deviation or number (%).

DCI = distal contractile integral; IRP = integrated relaxation pressure; DL = distal latency; LES = lower esophageal sphincter.

\*Patient group excluding ballooning procedure.

<sup>†</sup>Patient group including ballooning procedure.

#### Table 4. Pre- and postoperative 24-hour pH monitoring

Variables		Group A* (n=7)		Group B <sup>†</sup> (n=9)			
	Preoperative	Postoperative	P-value	Preoperative	Postoperative	P-value	
DeMeester score	6.50±5.52	11.61±12.66	0.360	7.02±6.36	21.92±36.17	0.210	
Acid exposure time							
Total	$1.46 \pm 1.48$	2.64±3.26	0.420	$1.49 \pm 1.48$	5.61±10.17	0.240	
Upright	2.01±1.90	4.50±5.50	0.330	$1.92 \pm 1.82$	8.02±12.93	0.190	
Supine	0.50±0.73	0.87±2.17	0.620	0.73±1.10	$1.68 \pm 3.34$	0.280	
No. of reflux							
Total	29.29±27.13	14.43±11.82	0.200	26.67±25.43	$71.22 \pm 171.98$	0.490	
Upright	22.29±18.78	10.86±10.30	0.220	20.22±17.81	63.44±159.84	0.260	
Supine	7.14±12.48	3.57±3.87	0.340	6.56±11.10	7.78±12.55	0.830	

Values are presented as mean ± standard deviation.

\*Patient group excluding ballooning procedure.

<sup>†</sup>Patient group including ballooning procedure.



**Fig. 1.** The high-resolution manometry result of the patient with gastroesophageal junction cancer. The newly formed LES is distinguishable. After swallowing, DL and DCI stayed in the reference range, and normal peristalsis of the esophagus is noted.

UES = upper esophageal sphincter; DCI = distal contractile integral; DL = distal latency; LES = lower esophageal sphincter.

HRM, we can observe a newly formed LES. Following swallowing, the DCI value of 941.3 mmHg·cm·s and DL of 7.5 seconds remained within the reference range. The esophagus exhibited normal peristaltic movement.



## **DISCUSSION**

For many surgeons, it was challenging to determine whether total gastrectomy was the only option for early gastric cancer and benign lesions located at the proximal 1/3 of the stomach or around the GEJ. The higher morbidity rate and the possibility of worsened quality of life after the surgery are the main reasons that prompt surgeons to opt for proximal gastrectomy instead of total gastrectomy [21,22]. Although proximal gastrectomy offers advantages in terms of nutrition and preservation of the remnant stomach's function [8,9,23], postoperative reflux esophagitis is a significant concern that can hinder patients' quality of life [6,7].

During proximal gastrectomy, the diaphragmatic crura and phrenoesophageal ligament, which are key components of LES, are easily damaged during the anastomosis process. Therefore, it is meaningful to use an anastomosis method that could preserve the crucial LES function during proximal gastrectomy.

Several methods have been introduced to prevent reflux esophagitis. A recent systematic review identified 5 types of anastomosis: simple esophagogastrostomy, tube-like esophagogastrostomy, jejunal interposition, double tract method, and jejunal pouch interposition. The first 2 involve anastomosis between the esophagus and stomach, and reflux esophagitis rates were reported to be between 28.6% and 10.7%. Alternatively, the jejunum can be used for anastomosis. The occurrence rates of reflux esophagitis for patients with jejunal interposition and jejunal pouch formation were 4.5% and 10%, respectively. The double-tract method also showed a reflux esophagitis rate of approximately 5% [24]. Unlike other methods, DFT creates a new LES instead of preserving the original LES. The pre- and postoperative function of the LES should be thoroughly evaluated and compared to determine if this newly formed LES is functionally acceptable. This may be challenging with a single diagnostic tool. Therefore, multiple diagnostic tools should be used simultaneously to evaluate the LES function, including EGD, HRM, and impedance pH monitoring. EGD allows for direct visualization of reflux esophagitis and other structural deformities such as Barrett esophagus or hiatal hernia. HRM enables measurement of LES pressure and observation of continuous steps in esophageal peristalsis and relaxation of the LES. HRM is also useful in diagnosing various esophageal motility disorders and outlet obstructions. Impedance pH monitoring allows us to count the number of reflux episodes and AET, as well as calculate DMS. With DMS, we can diagnose patients who have reflux despite having normal LES pressure. Combining these 3 tests makes it much easier to evaluate the dynamic function of the LES. When we examine the results of our study, it is noteworthy that all patients exhibited Hill's grade I or II following the surgery. Prior to the operation, 3 patients displayed Hill's grade III, but the grade improved post-surgery. Upon individual comparison of each patient, none exhibited a worsening hiatal hernia. Additionally, none of the patients experienced reflux esophagitis. These findings reinforce the preserved functionality of the newly created LES. With the HRM data, we can initially observe the pressure of the newly formed LES. A normal LES typically exhibits pressure ranging between 15 and 30 mmHg. In our study, Group A and Group B exhibited LES pressures of 22.24 (±19.93) mmHg and 19.97 (±18.03) mmHg, respectively, which fall within the reference range [19]. In addition to the pressure itself, the relaxation that occurs after swallowing is also an important factor when evaluating the functional aspect of the LES. HRM parameters related to relaxation include IRP and DL. IRP reflects the normal relaxation of the GEJ in response to swallowing. In our data, the IRP values were 10.26 in Group A and 8.33 in Group B, both of which were within the reference range. DL represents the interval between upper esophageal sphincter and



contractile deceleration point, which is located 3 cm above the proximal margin of the LES. If DL is less than 4.5 seconds, it may indicate a premature or spastic contraction [19]. The DL values in both groups were also within the reference range. The average DMS in Group A was 11.61 (±12.66), while in Group B it was 21.92 (±36.17). In Group B, the DMS value was outside the normal range but fell within the cut-off range for mild gastroesophageal reflux disease (GERD) [20]. The average value increased after including the values of 2 patients with ballooning. Despite the high DMS and AET values of these 2 patients, their flap valve morphology (Hill's grade) remained intact after dilation. Symptomatically, one patient remained asymptomatic and the other patient's GERD symptoms were easily controlled with proton pump inhibitor.

One limitation of this study is that it is a pilot study with a limited number of patients, focusing on the functional outcomes of LPG with DFT. Further large-scale studies are needed to confirm our findings.

DFT was useful in preserving LES function after LPG. However, larger-scale studies are needed to confirm this finding.

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