



## Prolapse gastropathy syndrome may be a predictor of pathologic acid reflux

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the PGS group and 76.2% (16/21) of the EE group demonstrated pathologic acid reflux (DeMeester score > 14.72), there was no statistically significant difference between the two groups in the incidence of pathologic acid reflux ( $P = 0.11$ ).

**CONCLUSION:** There was no statistically significant difference in pathologic acid reflux between the PGS and EE group. These data suggest that endoscopically diagnosed PGS might be a predictor of pathologic acid reflux.

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**Key words:** Prolapse gastropathy syndrome; Pathologic acid reflux; Erosive esophagitis; Ambulatory esophageal pH monitoring; Retching

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### Abstract

**AIM:** To assess the occurrence of gastric acid reflux into the esophagus in endoscopically confirmed prolapse gastropathy syndrome (PGS).

**METHODS:** Using ambulatory esophageal pH measurement (BRAVO™ wireless esophageal pH monitoring system), twenty-six patients with PGS were compared with twenty-one patients with erosive esophagitis (EE) as controls. We assessed several reflux parameters, including the percentage of total time at pH < 4, and the DeMeester score.

**RESULTS:** There were no statistical differences between the PGS group and the EE group as to mean age, sex ratio and pH recording time. The EE group showed more severe reflux than the PGS group, as evaluated in terms of the longest duration of reflux, the number of reflux episodes, the number of reflux episodes lasting > 5 min, the total time with pH < 4 during acid reflux episodes, and the DeMeester score, but none of these parameters showed statistically significant difference. Although 53.8% (14/26) of

### INTRODUCTION

In 1984, Shepherd<sup>[1]</sup> proposed the term “prolapse gastropathy syndrome (PGS)”, defining the diagnostic criteria for PGS as persistent and recurrent retching symptoms combined with hematemesis or abdominal pain, an endoscopic finding of prolapse of tense, inflamed, congested gastric mucosa into the esophageal lumen during retching, and an unusually strong gag and retch at endoscopy. PGS has been considered as one of the causes of upper gastrointestinal bleeding<sup>[2-6]</sup>. In addition, it has been regarded as esophageal pseudotumor<sup>[7]</sup> and retrograde gastroesophageal intussusception<sup>[8]</sup>, combined with several severe complications such as Mallory-Weiss syndrome and esophageal rupture<sup>[9]</sup>. Besides the above conditions, it is thought that gastric acid might be regurgitated into the esophagus along with prolapsed gastric mucosa.

However, there have been no studies of pathologic gastric acid reflux into the esophagus associated with PGS. Therefore, we investigated whether gastric acid into the esophagus may occur in endoscopically confirmed PGS.

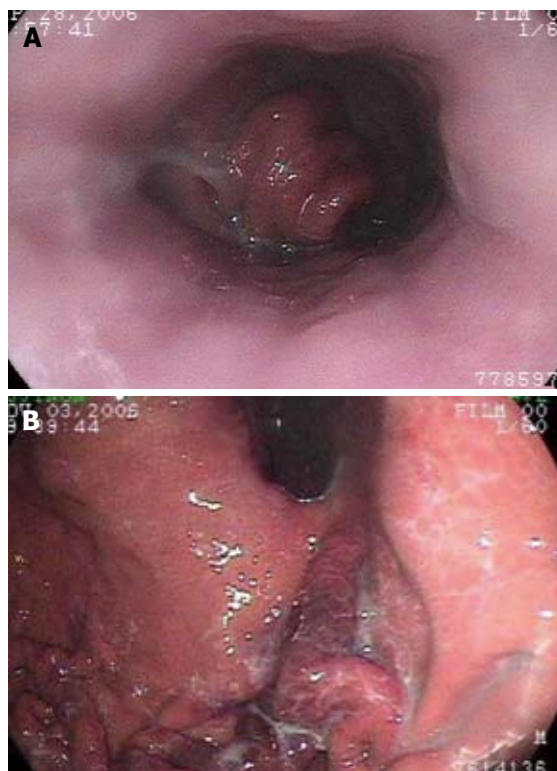
## MATERIALS AND METHODS

### Subjects

Subjects were selected from patients undergoing upper endoscopy at the gastrointestinal endoscopy center of Uijeongbu St. Mary's Hospital as part of a medical checkup or because of upper abdominal discomfort between May 2005 and May 2006. All patients with endoscopically confirmed PGS and erosive esophagitis (EE) were considered for inclusion in the study. Written informed consent for participation in the study was obtained from all patients. We prospectively enrolled 47 patients in two groups. The inclusion criteria for the PGS ( $n = 26$ ) group were endoscopically confirmed prolapse of inflamed gastric mucosa into the esophageal lumen during retching and symptoms of recurrent retching and nausea over 3 mo. Patients were excluded if they had endoscopically confirmed esophagitis or hiatus hernia, or were alcohol or drug abusers, pregnant, or obese (BMI > 25). The inclusion criterion for the EE group ( $n = 21$ ) was evidence of grade A or B (Los Angeles Classification) esophagitis at endoscopy. There was no specific exclusion criterion for the EE group. Endoscopic procedures were performed with videoendoscopes (GIF-Q260, GIF-XQ260, Olympus Optical Co. Ltd, Tokyo, Japan, EG-450WR5, Fujinon Corporation, Saitama, Japan).

### 48-hour esophageal pH measurement

All patients were studied after discontinuation of histamine-receptor antagonists, proton pump inhibitors, and prokinetics for at least 7 d. The BRAVO wireless esophageal pH monitoring system (Medtronic, Minneapolis, MN, USA) was used to measure esophageal pH in both groups within one week of gastroscopy. During gastroscopy, all subjects were assessed in order to locate the pH electrode exactly between the squamocolumnar junction and the incisors. According to the manufacturer's instructions, the pH electrode was passed through the mouth and positioned 6 cm above the squamocolumnar junction. In order to maintain this position, a vacuum pump was connected to apply suction to the esophageal wall. Successful capture of the esophageal mucosa was assumed when the vacuum gauge on the pump stabilized at a value of > 510 mmHg for 30 s. Before the pH capsule was inserted, it was calibrated with the receiver in pH buffer solutions of pH 7.01 and pH 1.07 at room temperature. During the 48 h pH-recording period, patients were asked to keep a detailed diary of activity, food intake, symptoms, wake and sleep periods and posture. Upon completion of the study, the pH monitoring tracings were analyzed using Polygram™ NET software (Medtronic, version 4.01). For each patient, the following reflux parameters were



**Figure 1** Endoscopic finding of the prolapse gastropathy syndrome group. **A:** Inflamed gastric mucosal prolapse viewed during retching; **B:** Congested and inflamed gastric mucosa secondary to prolapse gastropathy viewed in the gastric fundus.

determined: percentage of total time at pH < 4; upright time at pH < 4; supine time at pH < 4; the total number of reflux episodes; the number of reflux episodes longer than five minutes; and the mean duration of reflux episodes. A DeMeester score > 14.72 was defined as pathologic acid reflux. If the pH capsule detached within 16 h, it was reinserted and recorded again 2 wk later.

### Statistical analysis

Data presented in this manuscript are expressed as mean  $\pm$  SD. Comparisons between groups were performed using unpaired Student's *t* test, Fisher's exact test and chi-square test. A *P* value < 0.05 was considered as indicating statistical significance. All statistical analyses were performed using SPSS 11.0 for Microsoft Windows (Chicago, IL, USA).

## RESULTS

Forty-seven patients were included in the study, 26 patients with PGS and a control group of 21 patients with EE. The patients in the PGS group had a characteristic gastric mucosal prolapse due to retching (Figure 1A) and severe mucosal congestion and localized mucosal inflammation in the fundus (Figure 1B). Among the patients of the EE group, 17 (80%) showed grade A esophagitis and 4 (20%) showed grade B. The two groups were comparable in terms of mean age ( $41.5 \pm 6.7$  years for the PGS group and  $46.9 \pm 11.7$  years for the EE group) and gender ratio (male/female, 15/11 and 15/6,

**Table 1** Clinical characteristics and reflux parameters of patients in the PGS and the erosive esophagitis (EE) groups

	PGS group (n = 26)	EE group (n = 21)	P value
Age (yr)	41.5 ± 6.7	46.9 ± 11.7	0.08
Gender (male/female)	15/11	15/6	0.33
Mean recording time (h)	41.9 ± 5.9	40.9 ± 6.1	0.57
Number of reflux episodes	77.3 ± 46.4	98.2 ± 56.5	0.17
Number of long reflux episodes (> 5 min)	5.6 ± 4.0	8.5 ± 6.8	0.1
Duration of longest reflux episode (min)	19.6 ± 13.6	24.3 ± 15.7	0.28
Time at pH < 4 (min)	123.2 ± 93.6	173.7 ± 105.4	0.09
Total time of pH < 4 (%)	5.1 ± 4.5	6.9 ± 3.9	0.16
Erect time of pH < 4 (%)	5.6 ± 4.8	7.1 ± 4.2	0.08
Supine time of pH < 4 (%)	4.3 ± 3.2	5.0 ± 4.1	0.09
DeMeester score	15.9 ± 12.5	20.7 ± 10.8	0.17
Early detachment of Bravo wireless capsule	2 (7.7%)	0 (0%)	0.49

respectively) ( $P > 0.05$ ). Data from pH recording of the two groups are shown in Table 1. The mean recording time for the two groups was  $41.9 \pm 6.7$  h for the PGS group and  $40.9 \pm 6.1$  h for the EE group ( $P > 0.05$ ). The results of parameters of reflux in the PGS and EE groups showed no statistically significant differences in the percentage of total time at pH < 4 ( $5.1\% \pm 4.5\%$  and  $6.9\% \pm 3.9\%$ , respectively), the total number of reflux episodes ( $77.3 \pm 46.4$  and  $98.2 \pm 56.5$ , respectively), the number of reflux episodes longer than five minutes ( $5.6 \pm 4.0$  and  $8.5 \pm 6.8$ ), the duration of the longest reflux ( $19.6 \pm 13.6$  min and  $24.3 \pm 15.7$  min), total duration of time with pH < 4 ( $123.2 \pm 93.6$  min and  $173.7 \pm 105.4$  min), or DeMeester score ( $15.9 \pm 12.5$  and  $20.7 \pm 10.8$ ). As far as the incidence of pathologic acid reflux (based on DeMeester score > 14.72) is concerned, there was no significant difference between the PGS group (14/26 or 53.8%) and the EE group (16/21 or 76.2%) ( $P > 0.05$ ). Three patients developed complications related to the pH recording procedure. One patient in the PGS group experienced severe epigastric pain 48 h after placement of the pH capsule that resolved spontaneously. In two patients (7.7%) of the PGS group, early detachment of the pH capsule occurred as identified by a persistent decrease of pH to close to 2 followed by a rise above pH 7 after passage through the pylorus. For these patients, capsules were reinserted 2 wk later and pH recording was successful over 40 h.

## DISCUSSION

Retrograde prolapse of an area of gastric mucosal from the proximal stomach into the distal esophagus can occur during retching or vomiting and can result in prolapse gastropathy and bleeding. In 1984, Shepherd<sup>[1]</sup> proposed the term “prolapse gastropathy syndrome” and reported 22 patients who presented with epigastric pain alone or with hematemesis associated with a previous history of recurrent early morning retching or postprandial retching. He defined the characteristic endoscopic finding in these patients as a knuckle of inflamed and sometimes bleeding gastric mucosa in the proximal stomach several centimeters distal to the gastroesophageal junction that repeatedly prolapsed

into the esophageal lumen during retching<sup>[2,10,11]</sup>. The incidence of PGS has been reported to be 0.4%-2.4% in the general population, and it has been described in almost 2% of adults who undergo endoscopy for evaluation of hematemesis<sup>[1,12,13]</sup>. The mechanism of PGS is obscure although various factors such as relaxation of the esophagogastric junction, excessive redundancy of the gastric mucosa, retrograde peristalsis of the stomach and repeated regurgitation and vomiting have been suggested<sup>[7,14]</sup>. In this study, we investigated whether acid reflux into the esophagus may occur in PGS patients, because it is likely that regurgitation of acid accompanies the prolapsed mucosa. PGS patients were selected according to Shepherd's diagnostic criteria<sup>[1]</sup>. Patients with endoscopically confirmed esophagitis or hiatus hernia, who were alcohol or drug abusers, pregnant women, or obese (BMI > 25), were excluded to eliminate other factors that may contribute to pathologic acid reflux. In addition, a wireless ambulatory pH monitoring device was used rather than a traditional catheter-based esophageal pH monitoring system, because more throat and swallow discomfort, which might induce retching and pathologic acid reflux in PGS patients, has been reported with the catheter type than with the wireless monitoring device<sup>[15,16]</sup>. EE patients were chosen as a positive control for acid reflux because nonerosive gastroesophageal reflux disease (NERD) is often not related to pathologic acid reflux<sup>[17-20]</sup>.

Although, based on the DeMeester score, the positive rate of pathologic acid reflux in the EE group was higher than in the PGS group (76.2% *vs* 53.8%), our data show a meaningful rate of pathologic reflux in PGS patients, based also on the fact that we excluded other possible factors leading to reflux. In previous reports, hiatus hernia, which has been regarded as predictor of gastroesophageal reflux disease (GERD)<sup>[21,22]</sup> and NERD, revealed incidences of acid reflux of 26%-57%<sup>[23,24]</sup> and 40%-63%<sup>[25,26]</sup>, respectively. By comparison with these previous reports, the incidence of pathologic acid reflux in the PGS group is substantial.

With respect to complications associated with wireless pH recording, epigastric pain developed in one PGS patient 48 h after placement of the pH capsule that spontaneously resolved, and might be associated



with esophageal ulceration after placement of the pH capsule<sup>[27]</sup>. In addition, the pH capsule detached early in two patients of PGS group (7.7%, 2/26) but there was no case of detachment in the EE group. The detachment rate of the pH capsule in the PGS group was higher than in previous studies [3.2% (7/217), 3.7% (3/80)]<sup>[28,29]</sup>. The early detachment of the pH capsule may result from the prolapsed mucosa striking the attached pH capsule, meaning that an increased possibility of early detachment should be considered in PGS. However, further studies are necessary to confirm this.

Until now, there has been no report of the long-term prognosis for PGS patients, and it is not known whether long-lasting exposure of the esophagus to acid in PGS would progress to EE, esophageal stricture, Barrett's esophagus or other complications of GERD. Moreover, it is unknown whether a proton pump inhibitor or other medication is necessary to inhibit acid reflux in PGS patients. However there have been reports of a relationship between prolonged acid exposure and the degree of esophageal injury<sup>[30,31]</sup>, while recent cohort studies with prolonged follow-up showed progression from NERD to EE and from uncomplicated to complicated GERD<sup>[32,33]</sup>. We therefore recommend future studies to observe disease progression and response to medication in PGS over a long duration.

In conclusion, there was no statistically significant difference between PGS and EE groups in reflux parameters and presence of pathologic acid reflux. By comparison with previous reports of acid reflux in hiatus hernia and NERD, the incidence of pathologic acid reflux in the PGS group is substantial. This result suggests that PGS might be a predictor of pathologic acid reflux.

## COMMENTS

### Background

Prolapse gastropathy syndrome (PGS) occurs in patients with prolonged retching and vomiting. This disease is a clinical syndrome involving the invagination of part of the gastric mucosa into the lower esophagus, resulting in well demarcated hemorrhagic mucosa and severe mucosal congestion. Excessive gastric redundancy and prolapse of the mucosa may contribute to extended acid reflux of the esophagus. We aimed at investigating the acid reflux parameters in PGS compared with endoscopically confirmed erosive esophagitis.

### Research frontiers

There have been several studies and case reports about PGS which are focused on upper gastrointestinal bleeding.

### Innovations and breakthroughs

It seems to be that gastric acid might be regurgitated into the esophagus along with prolapsed gastric mucosa. However, there has been no study of acid reflux associated with PGS. This study is the first one designed to investigate the presence of pathologic acid reflux in PGS using the BRAVO wireless esophageal pH monitoring system to prevent acid reflux caused by pH monitoring probe of conventional method.

### Applications

Pathologic acid reflux in PGS may contribute to patient symptoms and progression to erosive esophagitis. Based on this study, the effectiveness of proton pump inhibitors in PGS will be considerable.

### Peer review

This is the first report designed to investigate the presence of pathologic acid

reflux in PGS. It concludes that the parameters of pathologic acid reflux in PGS are not different from those of erosive esophagitis. This result suggests that PGS may be a predictor of pathologic acid reflux.

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