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ORIGINAL ARTICLE

Duodenogastric Reflux: Proposed New Endoscopic Classification in Symptomatic Patients

Wei-Kuo Chang[1], Chih-Kung Lin[2], De-Chuan Chuan[3], You-Chen Chao[4,5]

[1]Department of Internal Medicine, Division of Gastroenterology, National Defense Medical Center, Tri-Service General Hospital, Departments of [2]Pathology and [3]General Surgery, National Defense Medical Center, Tri-Service General Hospital, [4]Division of Gastroenterology, Department of Internal Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, [5]School of Medicine, Tzu Chi University, Taiwan, Republic of China

Background: Duodenal contents reflux through the pylorus into the stomach can cause chronic gastritis and gastric cancer. This study aims to propose a new classification of endoscopic findings of duodenogastric reflux (DGR) in symptomatic patients. **Patients and Methods:** Eighty-eight patients with symptoms of DGR were included. Endoscopic findings, *Helicobacter pylori*, and mucosa pathological were recorded. Hepatobiliary scintigraphy was performed to quantify the DGR. **Results:** Among the 88 patients, 41 patients had normal mucosa (control group), 36 patients had bile lake (BL) (Group A), and 11 patients had bile stain (BS) (Group B). Group A significantly increases in postprandial DGR at 50 and 60 min. Group B significantly increases in fasting DGR at 50 and 60 min and postprandial DGR at 30, 40, 50, and 60 min. Group A and Group B had significant high intestine metaplasia and mucosal inflammation score than those in control group. Group B had a significantly higher incidence of gastric polyp than those patients in Group A and control group. **Conclusions:** Endoscopic findings of BS increased both fasting and postprandial DGR. BL had significant increased postprandial DGR. DGR increased the intestine metaplasia, mucosal inflammation, and gastric polyp in the stomach.

Key words: Duodenogastric reflux, gastritis, cholecystography, gastric polyp, *Helicobacter pylori*

INTRODUCTION

Duodenal contents reflux through the pylorus into the stomach is a physiological phenomenon that occur in the early morning, postprandial periods, and during endoscopy examination.[1,2] Long-term duodenogastric reflux (DGR) can cause pathological conditions such as chronic gastritis, foveolar hyperplasia, intestinal metaplasia, gastric dysplasia, gastric polyp, and gastric cancer.[3-7]

Characteristic DGR is the diagnosis by the presence of endoscopic observation of a large bile lake (BL) in the stomach with symptoms of nausea, vomiting, epigastric pain, and abdominal fullness.[1,3] However, clinical symptoms are not specific in the diagnosis of DGR.[8,9] Traditional endoscopic observation of BL [Figure 1b and c] could not provide as a standard tool to describe the endoscopic finding of excessive DGR.[1] Evaluation of DGR by endoscopic observation has several advantages, including the direct visualization of the excessive DGR, gastric mucosa erosion or ulceration, gastric polyp, and the feasibility for biopsy and pathological examination.

We hypothesis that endoscopic finding of bile stain (BS) [Figure 1d] in the stomach indicates the retention of a high concentration bile juice, leading to prolonged contact within the gastric lumen and resulting in possible pathological gastric mucosal changes. We proposed a new classification of endoscopic finding that bile juice and BS retention reflect the different severity of DGR. In this study, we compared the DGR with hepatobiliary scintigraphic method and examined its effects on the gastric mucosal pathology in symptomatic patients.

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Corresponding Author: Prof. You-Chen Chao, Division of Gastroenterology, Taipei Tzu Chi Hospital, Taipei Branch, No. 289, Jianguo Road, Xindian City, Taipei, Taiwan, Republic of China. Tel: +886-2-8792-7137; Fax: +886-2-8792-7138. E-mail: chaoycmd@yahoo.com.tw

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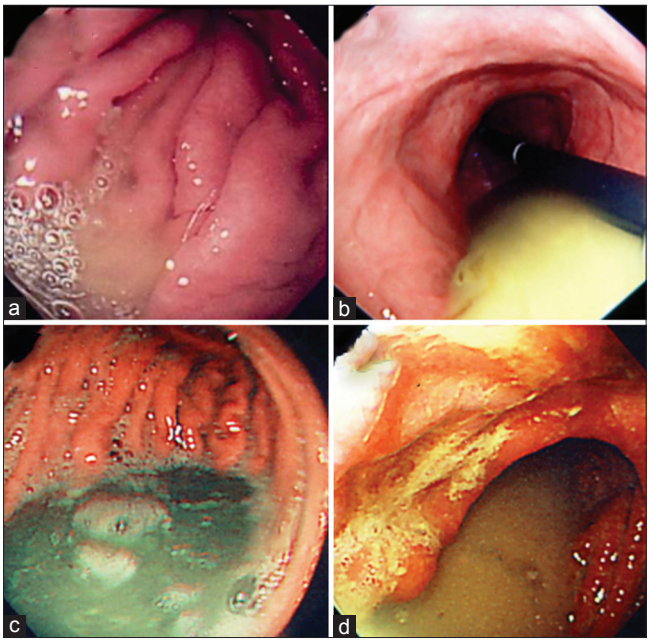

Figure 1: Endoscopic observation of gastric normal mucosa with clear gastric juice (a), yellowish bile lake (b), deep green bile lake (c), and sticky bile stain (d)

PATIENTS AND METHODS

Patient evaluation

Eighty-eight patients (56 men and 32 women; mean age 60 ± 18 years; age range 20–92 years) referred for DGR evaluation of symptoms such as nausea, vomiting, epigastric pain, and abdominal fullness were included in this study. All patients underwent upper gastrointestinal endoscopy, gastric mucosa pathological examination, and hepatobiliary scintigraphy. Patients taking nonsteroid anti-inflammatory drugs, steroid therapy, and those with excessive alcohol consumption were excluded. This study was approved by the Institutional Review Board of Tri-Service General Hospital, Taiwan. All patients were fully informed of the purpose of this study and had signed informed consent.

Endoscopic examination

All patients received an endoscopic examination by a senior gastroenterologist, who was unaware of the results of the hepatobiliary scintigraphy. Digitally recorded images were obtained by endoscopy (GIF 240, Olympus, Tokyo, Japan) using standardized white balance values. The patients were divided into three groups [Figure 1]: Control group, patients had endoscopic observation of gastric normal mucosa with clear gastric juice; Group A, patients had yellowish or green BL; and Group B, patients had sticky BS.

Helicobacter pylori and gastric mucosal pathology

During endoscopic examination, biopsy specimens were obtained from the antrum. *Helicobacter pylori* infection was assessed by the urease test and pathologic examination. Specimens obtained from gastric biopsy were fixed in formalin. For the purpose of detecting *H. pylori* infection, both the hematoxylin-eosin stain and the Giemsa stain were used. Histological severity of gastric mucosal inflammation was graded as 0 = normal, 1 = mild, 2 = moderate, and 3 = severe.[10]

Hepatobiliary scintigraphy

Each patient underwent overnight fasting prior to intravenous injection of 5–8 mCi Tc-99m-labeled diisopropyl iminodiacetic acid. After injection of the radiopharmaceutical, the Hawkeye system (GE Medical Systems, Milwaukee, WI, USA) obtained sequential abdominal images covering the liver, gallbladder, stomach, and bowel every minute for 60 min. Each patient then consumed a fatty meal (571 kcal, 29 g of fat, 61 g of carbohydrate, and 17 g of protein) consisting of one piece of bread with butter and 240 ml of whole milk. An additional 60 min of imaging (60 s/frame) was performed with the patients in the supine position. Quantitative DGR was calculated by measurement of the cumulative radioactivity over the gastric area in the hepatobiliary scintigraphy imaging study.[11]

Statistical analysis

The independent *t*-test was used to compare the differences in quantitative DGR hepatobiliary scintigraphy. The difference in gastric mucosal inflammation was calculated by the Mann–Whitney U-test. Odds ratio and 95% confidence intervals were calculated to determine the strength of the influence that each of the individual factor, such as endoscopic observed BL, BS, and *H. pylori* infection, may have on gastric polyp. Pearson Chi-square test was used to compare the frequency of variables in the patients with gastric polyp. Differences were considered statistically significant when $P < 0.05$.

RESULTS

Patients

Among the 88 patients, 25 patients had Billroth II, 6 patients had Billroth II with Braun's procedure, 17 patients had Roux-en-Y, and 2 patients had cholecystectomy. Thirty-eight patients did not receive previous abdominal surgery. The duration of symptoms prior to this study was 46 ± 27 months (range 2–89 months). Among the 88 patients, 41 patients had normal mucosa (control group), 36 patients had BL (Group A), and 11 patients had BS (Group B).

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Fasting duodenogastric reflux

Fasting DGR was compared among the three groups [Figure 2a]. Group B patients had significantly increased fasting DGR at 50 ($P < 0.05$) and 60 min ($P < 0.01$) when compared to the control group patients. Group A patients had no significant difference when compared to the patients in control group or group B.

Postprandial duodenogastric reflux

Postprandial DGR was compared among the three groups [Figure 2b]. Group B patients had significantly increased DGR at 30 ($P < 0.05$), 40 ($P < 0.01$), 50 ($P < 0.01$), and 60 min ($P < 0.01$) when compared to the control group. Group A patients also had significantly increased DGR at 50 ($P < 0.05$) and 60 min ($P < 0.01$) when compared to the control group. There were no significant differences as compared between Group A and Group B.

Helicobacter pylori and gastric mucosal pathology

The prevalence of *H. pylori* infection, foveolar hyperplasia, and dysplasia did not differ significantly among these three groups [Table 1]. Intestine metaplasia was observed in 12% (29/41) of the control patients, 53% (19/36) in Group A patients, and 55% (6/11) in Group B patients. Both Group A ($P = 0.023$) and Group B ($P = 0.016$) patients had significant high intestine metaplasia than those in control group. Both Group A ($P = 0.035$) and Group B ($P = 0.028$) patients also had significant high mucosal inflammation score than those in control group. On comparing the intestine metaplasia and mucosal inflammation between patients with Group A and Group B, there were no significant differences.

Table 1: Duodenogastric reflux and gastric mucosal pathology

	Control (n=41)	Group A (n=36)	Group B (n=11)	P
Helicobacter pylori infection (%)	6 (35)	10 (39)	6 (55)	NS
Foveolar hyperplasia (%)	6 (15)	7 (19)	3 (27)	NS
Dysplasia (%)	3 (7)	5 (14)	2 (19)	NS
Intestine metaplasia (%)	12 (29)	19 (53)	6 (55)	0.04
Inflammation score	1.0±0.8	1.4±0.7	1.6±0.9	0.03

NS = Not significant

Gastric polyp

Seven patients were found to have gastric polyp [Figure 3]. Gastric polyp was observed in 2% (1/41) of patients in control group, 6% (2/36) of patients in Group A, and 36% (4/11) of patients in Group B, respectively. Group B patients had a significantly higher incidence of gastric polyp than Group A patients (OR = 9.714, 95% CI = 1.479–63.806, $P = 0.021$) and those in control group patients (OR = 22.857, 95%CI = 2.215–235.820, $P = 0.005$).

DISCUSSION

Transit bile reflux is occasionally observed during endoscopy because the process of inserting an endoscope may generate retropulsive waves and lead to mild or sporadic DGR.[12] Traditional observation of BL in the stomach is considered as a poor indicator of DGR.[1] Stein *et al.* demonstrated a poor sensitivity (37%), specificity (70%), and positive predictive value (55%) in the endoscopic diagnosis of excessive DGR.[1]

The upper gastrointestinal endoscopy procedure is an invasive technique; therefore, there is a chance of inducing transit reflux by the procedure itself. However, BS indicates the retention of a high concentration and/or a large volume of bile juice in the stomach, leading to prolonged contact within the gastric lumen and resulting in pathological gastric mucosal changes. Therefore, our results showed the endoscopic observation of the BS, but not BL is associated with excessive DGR and confirmed by the scintigraphic method.

Scintigraphic method to demonstrate DGR using 99mTc is a physiological and quantitative method. Clinicians have used fatty meal to stimulate gallbladder contraction in

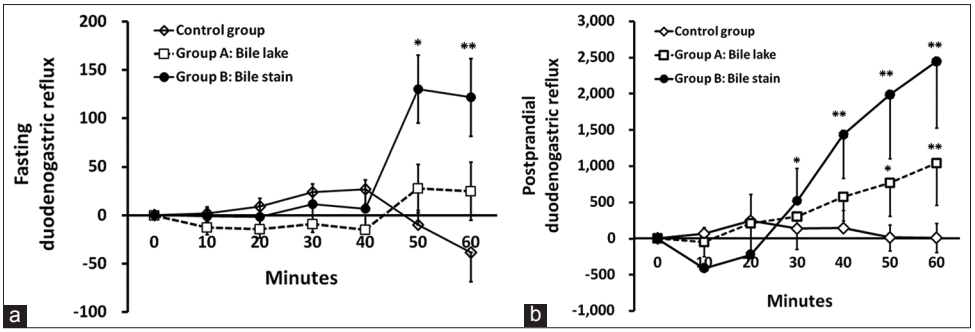

Figure 2: Fasting (a) and postprandial duodenogastric reflux (b) demonstrated in patients with endoscopic observation of gastric normal mucosa, bile lake, and bile stain (*<0.05; **<0.01)

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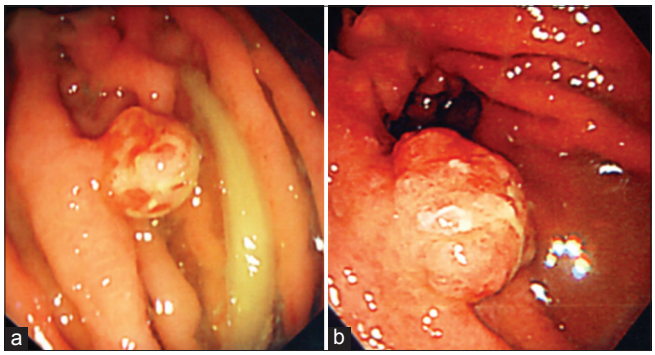

Figure 3: Endoscopic appearance of 1–2 cm gastric polyp with short stalk, mucosal congestion, superficial erosion, and friability in nonsurgically treated patients (a) and postgastrectomy patients (b)

conjunction with scintigraphy method.[11] Without gall bladder contraction stimulated by fatty meal, there was no sufficient radioactivity of bile contents regurgitation from duodenum into the stomach [Figure 2]. Our results showed the endoscopic observation of the BS, but BL is not associated with excessive DGR and confirmed by the scintigraphic method.

An ambulatory monitoring system, the Bilitec 2000, consists of a miniaturized fiberoptic probe and allows spectrophotometric measurement of luminal bilirubin concentration by detecting the absorption bands at 450 nm. [13] The time exposure to duodenal contents is measured and the bilirubin levels are monitored. Because most patients with excessive DGR have prior gastric surgery, interpretation of bilirubin in the stomach would be complex. Bilitec 2000 underestimates DGR by about 30% in acidic medium (pH < 3.5) and any food contents absorbing around 470 nm in the stomach may result in a false positive reading.[13,14]

Regurgitation of duodenal contents, including alkaline pancreatic–duodenal secretions, bile salts, and lysolecithin into the gastric cavity may disrupt the gastric mucosa barrier and damage the mucosa epithelium.[15] Excessive DGR results in accelerated regeneration of epithelium with histological appearance of foveolar hyperplasia and expansion of the smooth muscle fiber in the mucosa.[16,17] Patients with DGR had higher intensity of gastric mucosal inflammation.[18-20] Matsuhisa and Tsukui also showed that high concentrations of bile acids were shown to have an effect on the progression of intestinal metaplasia in *H. pylori*-negative patients.[18]

Gastric polyp is frequently found in patients with bile reflux gastritis after gastric surgery.[21] It is well known that gastric carcinomas may develop in the postgastrectomy stomach polyp.[22] The presence of bile acids in the gastric remnant may contribute to mucosal injury and may cause the risk of stump carcinoma.[23,24] Our data demonstrated that patients with BS had a significantly higher incidence of gastric polyp than patients with BL and those patients with normal mucosa.

CONCLUSION

Patients with endoscopic findings of BS had more severe excessive DGR. Endoscopic findings of BS suggested increased fasting and postprandial DGR. However, patients with endoscopic findings of BL had significant increased postprandial DGR. Patients with DGR increased the intestine metaplasia, severity of gastric mucosal inflammation, and incidence of gastric polyps in the stomach.

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Conflicts of interest

There are no conflicts of interest.

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