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Using the Updated Sydney System to Score Duodenogastric Reflux Disease in Taiwan: The Clinical Value of Reflux Gastritis Score and Bile Reflux Index

Chih-kung Lin[1], Hueng-Wei Gao[1], Shiou-Chi Cherng[2], Wei-Kuo Chang[3], and You-Chen Chao[3*]

[1]Department of Pathology; [2]Department of Nuclear Medicine; [3]Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China

Background: A new visual analog scale for grading variables has been incorporated into the updated Sydney System devised by Dixon et al. (1994), and it is consistent between observers with regard to all variables. In previous studies, the composite reflux gastritis score (RGS) and the bile reflux index (BRI) were significantly higher in duodenogastric reflux (DG reflux), postoperative, and GERD patients. **Methods:** The visual analog scale was used to calculate RGS and BRI simultaneously in DG reflux patients from one medical center in Taiwan. Eighty-eight patients with symptoms suggestive of DG reflux were enrolled in this study; 50 had previous gastric or biliary surgery, and 38 had no previous abdominal surgery. All patients underwent upper gastrointestinal endoscopy and pathologic gastric mucosa examination. **Results:** Bile lakes of gastric mucosa and severe reflux esophagitis were observed endoscopically. Biopsy specimens were taken from antrum or anastomosis of the gastric mucosa, and *H. pylori* infection was determined by a urease test. There was a weak association between RGS >9 and endoscopic bile lakes, and no significant differences were seen in BRI values. Nonsurgical RGS (mean 6.0) was half that of Dixon et al. (mean 12.0) and significantly lower (mean 5.3) in postoperative GERD patients. An RGS ≦6 weakly indicates increased prevalence of GERD; an RGS >6 indicates decreased prevalence of GERD. Between the two groups, the value of acute and chronic inflammatory cells was higher in postoperative GERD patients. **Conclusions:** Our results support the idea that RGS or BRI may not be good predictors in evaluating DG reflux patients.

Key words: RGS, BRI, updated Sydney System, GERD, DG reflux

INTRODUCTION

Reflux of alkaline duodenal contents through the pylorus into the stomach occurs during the early morning and postprandial periods and is occasionally observed during endoscopy[1,2]. This phenomenon is more common in patients who have undergone gastric surgery. However, excessive duodenogastric (DG) reflux can cause chronic gastritis, gastric ulcers, increased risk of gastric cancer[3,4], reflux esophagitis (RE), and Barrett's esophagus[5,6].

Endoscopic observation of a large bile lake in the stomach, antral mucosal erythema, friability, erosions, and ulcers in patients with nausea, vomiting, epigastric pain, and abdominal fullness have been suggested as clinical indicators of excessive DG reflux[1,3]. DG reflux can be determined objectively through hepatobiliary scintigraphy[7-9].

Distinctive histologic features of DG reflux include foveolar hyperplasia (FH), lamina propria vasodilatation and congestion (VC), edema (Ede), and a paucity of acute (AI) and chronic (CI) inflammatory cells. Using grades (0-3) for each of these features, a composite "reflux gastritis score" (RGS) was devised by Dixon et al. in 1986[5], comprising (FH+VC+Ede)—(AI+CI)+6 (ranging from 0 to 15). The mean reflux gastritis score was significantly higher in postoperative patients than in normal endoscopy and peptic ulcer patients. However, many subjects with a high RGS did not have bile reflux, so a more accurate bile reflux index (BRI), was devised by stepwise logistic regression analysis of the histologic grades used in the RGS together with intestinal metaplasia (IM) and H. pylori colonization (Hp) found in gastric biopsy. An index comprising (7×Ede)+(3×IM)+(4×CI)—(6×Hp) gave the best prediction of an elevated gastric-juice bile acid concentration[10]. To translate histopathologic observations into well-defined topographic patterns, or to use for comparison purposes, it is desirable to grade each relevant

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*Corresponding author: You-Chen Chao, Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, No. 325, Sec. 2, Cheng-Gong Road, Taipei 114, Taiwan, Republic of China. Tel:+886-2-8792-3311 ext 16731; Fax: +886-2-8792-7159; E-mail: lueshear@seed.net.tw

Table 1 Statistics of BRI, RGS, Operation, Bile lake and GERD in all patients.

	BRI	RGS	Operation		Bile lake		GERD	
			+	-	+	-	+	-
Count	88	88	50	38	48	40	66	22
Range	-14~35	2~11						
Mean (1SD)	12.2 (10.7)	6.0 (2.4)						

Table 2 Differences in BRI and RGS between Bile lake$^{(+)}$ and Bile lake$^{(-)}$ in all patients.

	BRI	RGS	RGS	
	(mean)	(mean)	>9	≦ 9
Bile lake				
+	11.9	6.3	7	41
-	12.5	5.8	1	39
	t=-0.26	t=0.92	Kendall's tau-b =0.21	
	P=0.80	P=0.36	P=0.033*	

*:P<0.05

feature using a standardized, reproducible scale. The updated Sydney System was devised by Dixon et al. in 1994[11]. Since then, a new visual analog scale for grading variables has been designed, and a set of guidelines has been created for its application. The visual analog scale is consistent among observers on all variables. In our study, we used the visual analog scale of the updated Sydney System to calculate the RGS and BRI on duodenogastric disease patients in one medical center and to analyze RGS and BRI with clinicopathologic parameters.

Fig. 1 Endoscopic observation of clear gastric juice (1A), yellowish bile lake (1B) and deep green bile lake (1C) in the stomach.

PATIENTS AND METHODS

Patients

Eighty-eight patients (56 men and 32 women; mean age 62±17 years; age range 20 to 92 years) with symptoms suggestive of DG reflux, such as nausea, epigastric pain, or biliary vomiting, were enrolled in this study in 2006 (Table 1). Fifty patients had previous gastric or biliary surgery (25, Billroth II; 6, Billroth II with Braun's procedure; 17, Roux-en-Y; and 2, cholecystectomy). Thirty-eight patients had not undergone previous abdominal surgery. All patients underwent upper gastrointestinal endoscopy and pathologic gastric mucosa examination. Patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) including acetylsalicylic acid, receiving steroid therapy, or who engaged in excessive alcohol consumption were excluded. This study was approved by the Institutional Review Board of Tri-Service General Hospital, Taiwan. Patients were fully informed about the purpose of this study, and informed consent was obtained from all subjects.

Endoscopic Examination

All patients received an endoscopic examination performed by a senior gastroenterologist. Observation of greenish or yellowish large bile lake (BL) of the gastric mucosa (Fig. 1) and the severity of reflux esophagitis (RE) were recorded. Four or more biopsy specimens were taken from the antrum or anastomotic site of the gastric mucosa, and *H. pylori* infection was determined by the urease test. The endoscopic grading of GERD was according to the Los Angeles Grading Scheme: grade A, one (or more) mucosal breaks no longer than 5 mm that do not extend between the tops of two mucosal folds; grade B, one (or more) mucosal breaks more than 5 mm long that do not extend between the tops of two mucosal folds; grade C, one (or more) mucosal breaks that are continuous between the tops of two or more mucosal folds but involve <75% of the esophageal circumference; grade D, one (or more) mucosal breaks that involve at least 75% of the esophageal circumference.

Grading Morphologic Variables

Specimens obtained from gastric biopsy were fixed in 10% buffered formalin, paraffin-embedded and 5- μM sections cut and stained with hematoxylin and eosin. The immunohistochemical stain for *H. pylori* was used to detect infection and colonization. A senior pathologist graded seven morphologic variables: (1) acute inflammation; (2) chronic inflammation; (3) H. pylori colonization; (4)

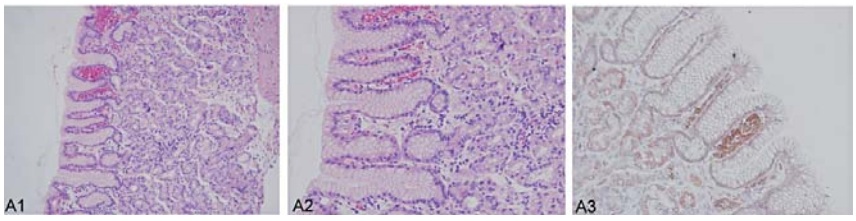

Fig. 2 Biopsy specimen showing mild foveolar hyperplasia (grade 1), mild stromal edema in the lamina propria (1), severe vascular congestion (3), paucity of chronic inflammation (3) and absence of polymorphs (3), and intestinal metaplasia (0) (A1, A2). No H. pylori infection was identified by immunohistochemical staining of Hp (A3). (A1: H&E X 200; A2: H&E×400; A3: I.H.C. ×400)

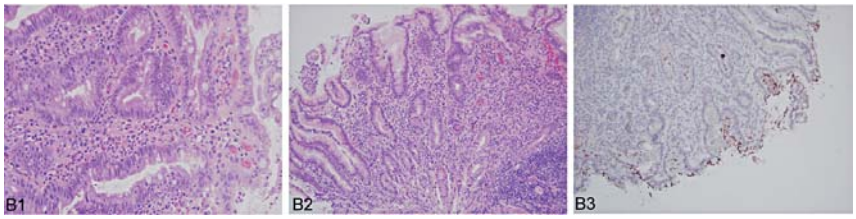

Fig. 3 Biopsy specimen showing mild foveolar hyperplasia (grade 1), mild stromal edema in lamina propria (1), severe vascular congestion (3), moderately chronic inflammatory cells (1), mild polymorphs (2) and mild intestinal metaplasia (1) (B1, B2) as well as moderate H. pylori colonization (2) as identified by immunohistochemical stain of Hp (B3). (B1: H&E×400; B2: H&E ×200; B3: I.H.C. ×200).

intestinal metaplasia; (5) foveolar hyperplasia; (6) edema of lamina propria; and (7) vascular congestion. Variables 1 to 4 were graded according to the visual analog scale of the updated Sydney System[11]. Variables 5 to 7 were graded according to Fig. 1 to Fig. 3 of Dixon et al.[2] A score from 0 (normal or absent) to 3 (severe) was allotted for each histologic feature, but acute and chronic inflammatory cells were graded separately and given scores that reflected their paucity; that is, 0 (severe increase) to 3 (normal or absent). Examples of histologic grading are shown in Figs 2 and 3. RGS and BRI were calculated for each patient.

Statistical Analysis

Statistical analysis was performed using Student's *t*-test, Chi-square test, and Kendall's tau-b correlation between groups. Statistical significance was determined by a *P* value less than 0.05. Tests were performed using SPSS version 10.0.

RESULTS

Correlation of Bile Lake with BRI and RGS in all Patients

The mean RGS was 6.3 (95% CI: 5.5-6.5), which was higher than 5.8 in bile lake negative patients but did not reach statistical significance. The mean BRI was lower (mean 11.9; 95% CI: 10.0-14.4) and lacked significant difference when compared with bile lake negative patients. Dixon et al. showed a significant increase of RGS (>10) in patients with increased bile acid concentration[5]. In our study, RGS was >9 in eight patients, and seven patients had endoscopic bile lake, showing significant correlation (Kendall's tau-b test: 0.21, $P < 0.05$); 80 patients had an RGS score of ≦ 9, with 41 having endoscopic bile lake. However, no correlation was seen in the BRI between the two groups of patients.

Correlation of Operation with Bile Lake, GERD, RGS and BRI Scores

We compared patients who had undergone abdominal surgery and subsequent bile lake, RGS and BRI scores, and correlation with reflux esophagitis RE (GERD). Data showed that the number of endoscopic bile lake or GERD patients was higher among those who had had abdominal surgery (24; 35, respectively), but significant differences were not found between the two groups of patients ($P = 0.07$; $P = 0.06$, respectively). In addition, we found that RGS values were half of those found in the study of Dixon et al.[5] (mean 6.0 in our study; 12.0 in Dixon et al.) among postoperative patients (data not shown).

Correlation between GERD and RGS, BRI in Postoperative Patients

Differences between RGS and BRI in postoperative GERD patients are shown in Table 3. RGS was significantly lower (mean 5.3, $P < 0.01$) in postoperative patients who suffered from reflux esophagitis, but BRI was not significantly higher (mean 13.2, $P > 0.05$). An RGS of ≦ 6 (22 of 27 patients) was associated with an increased prevalence of reflux esophagitis, and an RGS of >6 (12 of 23 patients) was associated with decreased prevalence of reflux esophagitis ($P < 0.05$). Neither the severity (grades A to D) of GERD nor the type of surgery performed was associated with the reflux gastritis score (data not shown). This is the first time that RGS showed significant association with GERD. We knew that the composite RGS was

Table 3 Differences in BRI and RGS between GERD(+) and GERD(-) postoperative patients.

	BRI	RGS	RGS	
	(mean)	(mean)	>6	≦ 6
GERD				
+	13.2	5.3	12	22
-	11.0	7.6	11	5
	t=0.66	t=-3.1	χ^2 =4.9	
	P=0.51	P=0.003*	P=0.027*	

*:P<0.05

Table 4 Differences in FH+VC+Oede, AI+CI and H.pylori between GERD(+) and GERD(-) postoperative patients.

	FH+VC+Oede	AI+CI	H. pylori	
	(mean)	(mean)	+	-
GERD				
+	3.9	4.6	11	23
-	4.6	3.2	7	9
	t=-1.2	t=3.3	χ^2 =0.61	
	P=0.24	P=0.002*	P=0.43	

*:P<0.05
Abbreviations: Foveolar hyperplasia, FH; Oedema, Oede; Vascular congestion, VC; Acute inflammation, AI; Chronic inflammation, CI.

calculated by (FH+VC+Ede)—(AI+CI)+6, and we separated the reflux gastritis score into (FH+VC+Ede) and (AI+CI) in the two groups, further analyzing the correlation between GERD and *H. pylori* infection. We found that AI+CI was significantly higher in GERD patients, indicating lower severity of acute and chronic inflammation ($P < 0.05$), but found a lack of association with *H. pylori* infection (Table 4).

DISCUSSION

Reflux of duodenal content into the stomach occurs during the early morning or the postprandial period[12,13]. However, excessive DG reflux is common in adults after gastric surgery, pyeloplasty, and cholecystectomy[14-17]. DG reflux also occurs in 30% to 40% of adult patients presenting with acid RE or GERD[18,19]. Excessive DG reflux has been associated with symptoms of epigastric pain, nausea, and bilious vomiting and has been implicated in the development of antral gastritis, alkaline esophagitis, gastric ulcers, intestinal metaplasia of the gastric mucosa, and esophageal or gastric adenocarcinoma[20-24]. Because symptoms are not specific, the clinical diagnosis of excessive DG reflux is based on endoscopic observation of a bile lake in the stomach, antral gastritis or ulceration, or the histologic documentation of foveolar hyperplasia, vascular congestion, lamina propria edema or chemical gastritis[5,25,26]. Both RGS and the more accurate BRI were devised by Dixon et al.[5,10] for predicting the prevalence of DG reflux and Barrett's esophagus. They found a significant difference in the incidence of hypochlorhydria and elevated bile acid concentrations between patients with an RGS above or below 10 as well as a BRI significantly higher in GERD patients than in nonulcer dyspepsia patients. However, poor agreement on RGS and BRI was noted. A new visual analog scale was introduced for grading variables in gastric disease, and because it had shown to be consistent among observers, it was incorporated into the updated Sydney System[11]. In our study, we used the visual analog scale of the updated Sydney System to simultaneously calculate RGS and BRI in DG reflux patients. We analyzed the correlation of both RGS and BRI with clinicopathologic parameters. We found a weak association between endoscopic bile lake and reflux scores above and below 9. In addition, a weak association was noted between the prevalence of GERD in postoperative patients and RGS results above and below 6, which could have resulted from a significantly higher value of AI+CI. The RGS is half (mean 6.0, range 2~11) that shown in Dixon's study[5]. We further analyzed each variable and compared the results with that of Dixon et al. Among our patients, results were significantly lower in patients with foveolar hyperplasia, vascular congestion, and paucity of inflammation, but not in patients with lamina propria edema (Table 5). This may have resulted from the use of the visual analog scale of the updated Sydney System, lack of scale for foveolar hyperplasia, vascular congestion and lamina propria edema, interobserver variation, different races, or effects of Asian dietary customs (such as herbal products or decoctions) on

Table 5 Differences in FH, VC, Oede and (AI+CI) values between two studies.

	FH Grade		Oede Grade		VC Grade		AI+CI Grade	
	3	<3	3	<3	3	<3	3	<3
Our study	7(20)[1]	81(68)	8(14)	80(74)	21(26)	67(62)	55(47)	33(40)
Dixon et al.	34(21)	61(74)	21(15)	74(80)	33(28)	62(67)	44(51)	51(43)
	χ^2 =20.36		χ^2 =5.80		χ^2 =2.60		χ^2 =4.82	
	P=0.000*		P=0.016*		P=0.11		P=0.028*	

[1]: Count (Expected Count)
*:P<0.05
Abbreviations: Foveolar hyperplasia, FH; Oedema, Oede; Vascular congestion, VC; Acute inflammation, AI; chronic inflammation, CI.

postoperative recovery. BRI did not show significant differences in observation of an endoscopic bile lake, postoperative or GERD patients, but a negative value for BRI (range from −14 to 35) was present in 13 of 88 patients, compared with that of Dixon et al. (range from 0 to 27)[10]. This phenomenon was caused by lower values of lamina propria edema, chronic inflammation, and intestinal metaplasia as well as higher *H. pylori* colonization. In fact, recognition of lamina propria edema and other histologic features of reflux gastritis are more difficult in *H. pylori* infected patients, indicating possible limited applicability of BRI values. In summary, BRI, a more accurate predictor of bile reflux, lacked any correlation between endoscopic bile lake, postoperative, or GERD patients, but RGS demonstrated a weak association with endoscopic bile lake or postoperative GERD patients. Our results support the idea that RGS or BRI may not be good predictors in evaluating DG reflux patients.

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