



A New Analysis for Old Problem of Bile Reflux

TO THE EDITOR: Factors that can contribute to bile reflux gastritis are generally categorized as primary biliary reflux and secondary biliary reflux after gastric resection with ablation of the pylorus. Primary biliary reflux is excessive bile in the duodenum retrograding to the stomach. Risk factors include gallbladder dyskinesia, gastric or duodenal dysmotility, and surgical resection such as cholecystectomy and sphincterotomy. Recently, a new analysis for the old problem of primary bile reflux gastropathy has been reported,¹ in which a total of 262 patients with functional dyspepsia (FD) were stratified into 3 cohorts: bile gastropathy (BG), non-bile gastropathy (NBG), and no gastropathy (NG). The evaluations based on phenotype, symptoms, endoscopic and histological changes, etc. were compared using chi-square test for continuous data, Kruskal–Wallis test (one-way analysis of variance) for continuous data, and multivariate regression for 2 binary modeling.

The findings of this study are mainly featured or established

with some characteristics to BG, in contrast to BNG and NG. Following aspects from BG, versus to BNG and NG, are significantly more severe or increased: (1) abdominal pain, (2) prevalence of cholecystectomy, (3) prevalence of gastric erythema in endoscopic examination, (4) prevalence of gastritis, (5) edema, and (6) chronic active inflammation on pathological examination. Indeed, this is a more comprehensive study, and its cohort analysis could be potentially informative in the diagnosis of bile reflux gastritis in clinical practice though it is not the criteria.

However, a few of concerns raised from this study may be worth to further discussing for clarification and understanding. First, the subjects included in the study were patients with FD, therefore, delayed gastric emptying was crucial and expected. In the literature, significantly longer delayed gastric emptying and higher bilirubin concentrations were observed in patients with bile reflux gastritis.^{2,3} The validation of the wireless motility capsule testing used in the study may need to adjust/compare with traditional or universally accepted measurements,⁴ since the supplementary results showing delayed gastric emptying in BG, NBG, and NG are respectively 38.6%, 40.4%, and 39.1% ($P = 0.981$), as seen in Table. At least, a further explanation on why there is no correlation with the degree of bile reflux among cohorts is expected by audiences. Second, the differential of heartburn was not discernable among the cohorts as seen in Figure. In the contrary, the amplitude of that from BG is obviously lower than other cohorts which looks different enough to be statistically significant. Then, the patients who did not have cholecystectomy could be more informative if such cohorts could be analyzed. Since the diagnosis of bile reflux gastritis is very challenging, any difference from BG, NBG, and NG may be guides for the diagnosis, treatment, and prognosis.

As commented,⁵ “role of bile reflux in functional dyspepsia: areas that need further research,” there are few studies on the association of bile reflux, FD, the severity of symptoms, and response to

Table. Assessment of Motility

Motility dysfunction	Bile gastropathy	Non-bile gastropathy	No gastropathy	<i>P</i> -value
Rapid gastric emptying	5.3	3.5	4.3	0.901
Delayed gastric emptying	38.6	40.4	39.1	0.981
Delayed small bowel transit	28.6	40.0	33.3	0.655
Delayed colonic transit	25.9	54.8	25.0	0.045
SIBO ^a	38.0	43.5	50.0	0.402
SIFO ^b	31.9	31.7	25.0	0.726

^aSmall intestinal bacterial overgrowth (SIBO) diagnosed by either duodenal aspirates ($\geq 10^3$ CFU/mL) or positive glucose breath test.

^bSmall intestinal fungal overgrowth (SIFO) diagnosed by duodenal aspirates (positive fungal cultures $\geq 10^3$ CFU/mL).

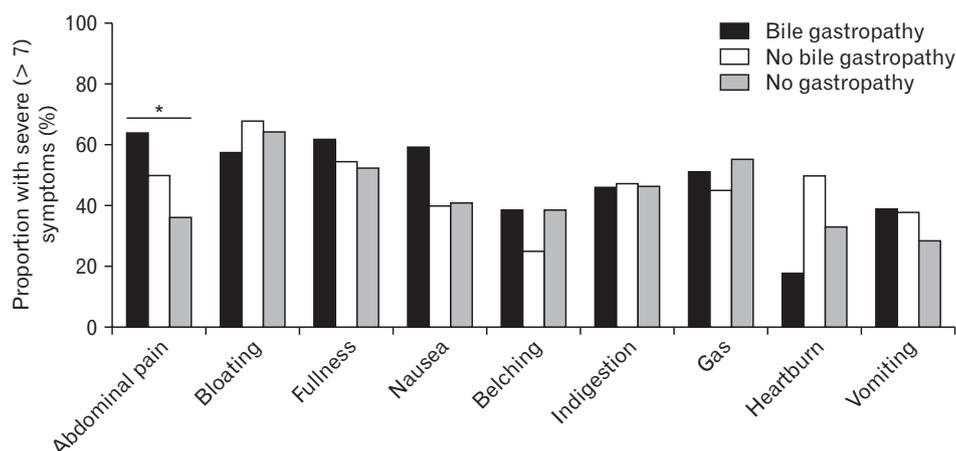


Figure. The distributions of patients' gastrointestinal symptoms in the 3 cohorts.

treatment in patients with FD undergoing cholecystectomy. As one of the important causes of FD, *Helicobacter pylori* was not documented in the study, which is not enough to reflect confounding factors in multivariate analysis. In addition, the severity of symptoms and response to treatment in patients with FD who underwent cholecystectomy needs further study to avoid a possibility of underestimating delayed gastric empty and heartburn.

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