

# Impact of Overlapping Functional Gastrointestinal Disorders on the Presentation and Quality of Life of Patients with Erosive Esophagitis and Nonerosive Reflux Disease

Shou-Wu Lee<sup>a, b</sup> Chi-Sen Chang<sup>a, b</sup> Han-Chung Lien<sup>a, c</sup> Yen-Chun Peng<sup>a, c</sup>  
Chun-Ying Wu<sup>a, c</sup> Hong-Zen Yeh<sup>a, c</sup>

<sup>a</sup>Division of Gastroenterology, Department of Internal Medicine, Taichung Veterans General Hospital, and  
<sup>b</sup>Department of Internal Medicine, Chung Shan Medical University, Taichung, and <sup>c</sup>Department of Internal  
Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC

## Key Words

Erosive esophagitis · Functional gastrointestinal disorder ·  
Gastroesophageal reflux disease · Nonerosive reflux  
disease · Quality of life

## Abstract

**Objective:** The aim of this study was to investigate the impact of overlapping functional gastrointestinal disorder (FGID) on the quality of life of patients with nonerosive reflux disease (NERD) and erosive esophagitis (EE). **Materials and Methods:** Data from patients with NERD and EE were collected between January 2009 and March 2010. These cases were further stratified into the subgroups of overlapping NERD-functional dyspepsia (FD), NERD-irritable bowel syndrome (IBS), EE-FD, EE-IBS, and NERD or EE alone according to the symptoms. All patients completed the modified Chinese GERDQ and the SF-36 questionnaires. **Results:** Of the 222 enrolled patients, 96 (43.2%) had NERD and 126 (56.8%) had EE. Overlap of FGID occurred in 43.8–45.8% of the NERD patients, and in 41.3–44.4% of EE cases. The impact of overlapping FGID on patient quality of life was greater in the patients with overlapping NERD-FD compared to those with

NERD alone (mean SF-36 total scores 59 vs. 72, adjusted  $p = 0.025$ ) and the cases with overlapping EE-FD compared to those with EE alone (mean SF-36 total scores 53.19 vs. 73.11, adjusted  $p = 0.047$ ). There were no significant differences between the individuals with overlapping NERD/EE-IBS and those with NERD/EE alone. **Conclusions:** There was a high prevalence of overlapping FGID, with both FD and IBS, among the GERD patients. The individuals with overlapping GERD and FD had lower quality of life scores than those with GERD alone.

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## Introduction

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders worldwide [1, 2]. According to the Montreal definition, GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms or complications [3]. Furthermore, GERD can be classified as erosive esophagitis (EE) or nonerosive reflux disease (NERD). EE is defined as an endoscopic esophageal mucosal break, while

**Table 1.** Basic characteristics of the NERD and EE patients

Variable	NERD (n = 96, 43.2%)		EE (n = 126, 56.8%)		p value
	n (%)	mean ± SD	n (%)	mean ± SD	
Mean age, years		42.25 ± 14.11		50.13 ± 18.40	0.015 <sup>b</sup>
Gender					0.286 <sup>a</sup>
Male	42 (43.8)		68 (54.0)		
Female	54 (57.2)		58 (46.0)		
Weight, kg		64.46 ± 11.93		63.98 ± 14.30	0.853 <sup>b</sup>
BMI		23.77 ± 3.33		23.14 ± 4.35	0.409 <sup>b</sup>
S/S duration, months		2.77 ± 4.18		2.69 ± 3.25	0.108 <sup>b</sup>
Hiatal hernia	24 (25.0)		38 (30.2)		0.548 <sup>a</sup>
FD	44 (45.8)		52 (41.3)		0.631 <sup>a</sup>
IBS	42 (43.8)		56 (44.4)		0.942 <sup>a</sup>

S/S = Symptoms and signs. <sup>a</sup> Pearson's  $\chi^2$  test. <sup>b</sup> t test.

NERD is determined by typical symptoms and minimal change on endoscopy.

Functional gastrointestinal disorder (FGID), such as functional dyspepsia (FD) or irritable bowel syndrome (IBS), is present in over 20% of the general population [2]. As defined by the Rome III criteria, FD is a disorder in which bothersome postprandial fullness or epigastric pain persists for 3 months, without evidence of structural disease. FD can be further divided into postprandial distress syndrome and epigastric pain syndrome according to symptom presentation. As defined by the Rome III criteria, IBS manifests as recurrent abdominal pain or discomfort with at least two of the following characteristics: (a) relief with defecation, (b) onset associated with a change in the frequency of stool and (c) onset associated with a change in the form of stool. The type of IBS is further divided into diarrhea, constipation and mixed [4].

According to previous studies, GERD patients were characterized by a higher prevalence of FGID [2, 5–7]. Both GERD and FGID have negative impacts on the daily lives of affected individuals, interfering with physical activity, impairing social functioning, disturbing sleep and reducing productivity at work. The aim of this study was to investigate the impact of overlapping FGID, including FD and IBS, on the presentations and quality of life of individuals with EE and NERD.

## Materials and Methods

Data of 222 consecutive patients in our hospital with GERD who presented with typical symptoms of acid regurgitation or heartburn sensation were collected between January 2009 and March 2010. The exclusion criteria were as follows: (a) GERD

combined with esophageal or gastric malignancy, (b) prior gastric surgery, (c) peptic ulcer disease, (d) use of chronic antacid medication, such as proton pump inhibitors or H<sub>2</sub>-receptor antagonists, for more than 2 months prior to enrollment, and (e) pregnancy.

The general data of the enrolled patients, including age, gender, body mass index (BMI) and symptom duration, were recorded. All patients underwent an open-access transoral upper gastrointestinal endoscopy, and details of gastroesophageal junction (GEJ) mucosal break or hiatal hernia in each case were collected.

The enrolled patients were stratified into two major groups according to endoscopic finding: EE and NERD. The cases with symptoms compatible with FD and IBS, diagnosed by the Rome III criteria, and no GEJ mucosal break, were assigned to the subgroups of overlapping NERD-FD and NERD-IBS, respectively. The cases with FD and IBS with mucosal break at GEJ confirmed by endoscopic findings served as the subgroups of overlapping EE-FD and EE-IBS, respectively.

All the enrolled patients were asked to fill out the modified Chinese GERDQ and the Short Form 36 (SF-36) questionnaires. The modified Chinese GERDQ includes questions on the frequency of symptoms of regurgitation and heartburn, graded on a 3-point Likert scale. Low, middle and high frequencies were classified, corresponding to at least once per month, at least once weekly and at least once daily, respectively [8]. The SF-36 questionnaire measures generic quality of life, which allows comparisons between different disease states. Two summary scores are also calculated from subject responses: the physical health score and the mental health score. Scores of the SF-36 range from 0 to 100 for each dimension as well as on the summary scales, with higher scores indicating better quality of life [9].

Data are expressed as the mean and standard deviation for each of the measured parameters. Gender, hiatal hernia and the ratio of overlapping FGID are expressed as a percentage of the total number of patients. Statistical comparisons were made using Pearson's  $\chi^2$  test to compare the effects of gender, hiatal hernia and ratio of FGID, while analysis of variance was used to analyze age, body weight, BMI, symptom duration and questionnaire scores. Conditional logistic regression was used to examine the above results after adjustment for confounding factors. A p value <0.05 was considered statistically significant.

**Table 2.** Basic characteristics of the NERD and/or FGID patients

	NERD-FD (n = 44, 45.8%)	NERD (n = 52, 54.2%)	p value	NERD-IBS (n = 42, 43.8%)	NERD (n = 54, 56.2%)	p value
Mean age, years	36.36±12.71	47.23±13.50	0.006 <sup>b</sup>	42.29±13.96	42.22±14.48	0.988 <sup>b</sup>
Gender			0.034 <sup>a</sup>			0.912 <sup>a</sup>
Male	12 (27.3)	30 (57.7)		18 (42.9)	24 (44.4)	
Female	32 (72.7)	22 (42.3)		24 (57.1)	30 (55.6)	
Weight, kg	60.50±11.62	67.81±11.35	0.033 <sup>b</sup>	60.67±11.21	67.41±11.84	0.060 <sup>b</sup>
BMI	22.55±3.14	24.75±3.20	0.023 <sup>b</sup>	22.62±3.39	24.62±3.08	0.044 <sup>b</sup>

Values represent mean ± SD or n (%). <sup>a</sup> Pearson's  $\chi^2$  test. <sup>b</sup> t test.

**Table 3.** Basic characteristics of the EE and/or FGID patients

	EE-FD (n = 52, 41.3%)	EE (n = 74, 58.7%)	p value	EE-IBS (n = 56, 44.4%)	EE (n = 70, 55.6%)	p value
Mean age, years	44.08±17.38	54.38±18.12	0.027 <sup>b</sup>	51.93±19.34	48.69±17.76	0.496 <sup>b</sup>
Gender			0.002 <sup>a</sup>			0.334 <sup>a</sup>
Male	16 (30.8)	52 (70.3)		34 (60.7)	34 (48.6)	
Female	36 (69.2)	22 (29.7)		22 (39.3)	36 (51.4)	
Weight, kg	58.88±15.46	67.57±12.42	0.022 <sup>b</sup>	59.82±11.83	67.31±15.37	0.058 <sup>b</sup>
BMI	21.87±5.05	24.05±3.56	0.065 <sup>b</sup>	22.13±3.99	23.97±4.50	0.097 <sup>b</sup>

Values represent mean ± SD or n (%). <sup>a</sup> Pearson's  $\chi^2$  test. <sup>b</sup> t test.

## Results

Of the 222 consecutive patients enrolled, 96 (43.2%) were stratified into the NERD group and 126 (56.8%) into the EE group. There were no significant differences in gender distribution, BMI, mean duration of GERD symptoms and ratio of hiatal hernia between these two groups, but patients with NERD were significantly younger than those with EE (mean 42.25 vs. 50.13 years,  $p = 0.015$ ; table 1).

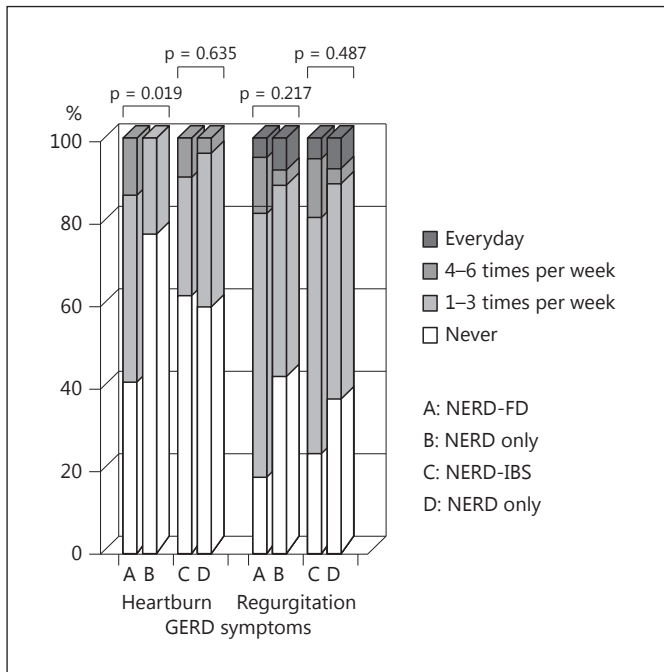
Among the 96 patients with NERD, 44 (45.8%) were classified into the overlapping NERD-FD and 42 (43.8%) into the overlapping NERD-IBS subgroups. Among the 126 patients with EE, 52 (41.3%) were classified into the overlapping EE-FD and 56 (44.4%) into the overlapping EE-IBS subgroups. The ratios of overlapping FGID in the cases with NERD and those with EE were similar.

The comparisons of NERD and EE patients with and without FGID are shown in tables 2 and 3. The individuals with overlapping NERD-FD tended to be significantly younger (mean age 36.36 vs. 47.23 years,  $p = 0.006$ ), predominantly female (72.7 vs. 42.3%,  $p = 0.034$ ) and had a

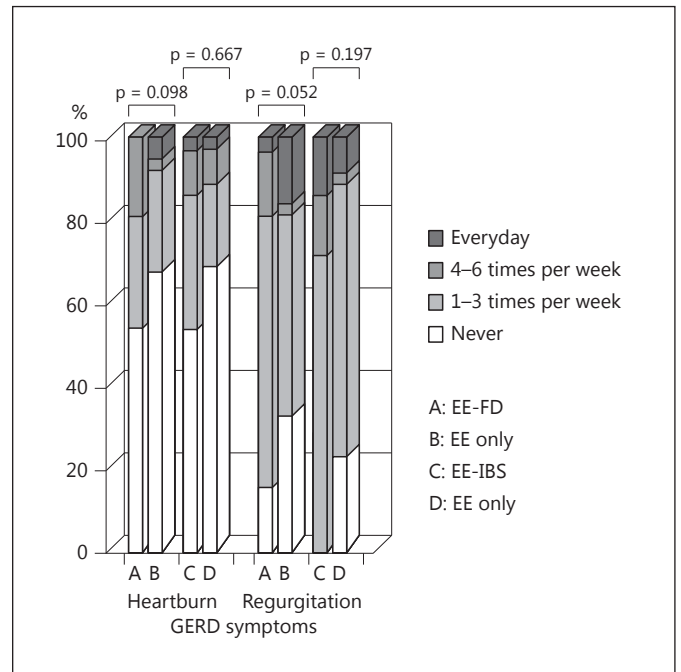
lower BMI (mean 22.55 vs. 24.75,  $p = 0.023$ ) than those with NERD alone. These findings were similar to those of the EE patients with and without FD (mean age 44.08 vs. 54.38 years,  $p = 0.027$ ; female ratio 69.2 vs. 29.7%,  $p = 0.002$ ; mean BMI 21.87 vs. 24.05,  $p = 0.065$ ). The cases with overlapping GERD-IBS and those with GERD alone were similar in age, gender distribution and BMI.

The frequencies of heartburn and regurgitation in NERD and EE patients, with or without FGID, scored by the modified Chinese GERDQ, are shown in figures 1 and 2. The results were similar except the patients with overlapping NERD-FD had more frequent episodes of heartburn than those with NERD alone ( $p = 0.019$ , adjusted  $p = 0.033$ ).

The quality of life scores of NERD and EE cases, measured by the SF-36, is shown in table 4. The patients with overlapping NERD-FD, compared with those with NERD alone, had significantly lower health scores (mean total scores 59 vs. 72,  $p = 0.009$ , adjusted  $p = 0.025$ ). Similarly, the cases with overlapping EE-FD had significantly lower scores than those with EE alone (mean total scores 53.19



**Fig. 1.** The frequency of heartburn and regurgitation, measured by the modified Chinese GERDQ, of the NERD patients with and without FGID.



**Fig. 2.** The frequency of heartburn and regurgitation, measured by the modified Chinese GERDQ, of the EE patients with and without FGID.

**Table 4.** SF-36 scores of the GERD patients

	Total scores	p value	Adjusted p value <sup>a</sup>
NERD-FD (n = 44)	59.00±16.05		
NERD (n = 52)	72.00±16.40	0.009	0.025
NERD-IBS (n = 42)	60.24±19.71		
NERD (n = 54)	71.00±13.74	0.041	0.061
EE-FD (n = 52)	56.19±15.61		
EE (n = 74)	73.11±15.46	0.001	0.047
EE-IBS (n = 56)	62.39±18.80		
EE (n = 70)	69.11±16.10	0.139	0.371

Values represent mean ± SD. <sup>a</sup> Adjusted for age and gender.

vs. 73.11,  $p = 0.001$ , adjusted  $p = 0.047$ ). However, the difference was not significant between the patients with overlapping NERD-IBS and those with NERD alone (mean total scores 60.24 vs. 71,  $p = 0.041$ , adjusted  $p = 0.061$ ), and the cases with overlapping EE-IBS and those with EE alone (mean total scores 62.39 vs. 69.11,  $p = 0.139$ , adjusted  $p = 0.371$ ).

## Discussion

The overlapping FD of 45.8% of all NERD patients, and 41.3% of all EE cases, was higher than the overlap of 8.1–17% in GERD patients, especially in NERD cases reported previously [2, 6, 7, 10]. The 43.8% prevalence of all NERD cases were within the range of 10.1–71% reported previously [6, 11, 12]. The high ratio of overlapping FGID and GERD in our study might be due to the hospital-based design, ethnic variation (Chinese population vs. Western population) or different definitions of FGID (Rome III vs. Rome II or I) adopted in individual studies.

The female predominance of the patients with overlapping FD-GERD, both NERD and EE, but not in the cases with overlapping IBS-GERD of this study, confirmed the findings of previous studies [13–15]. In our study, the probable reason for female predominance in those cases with overlapping FD-GERD could be that both GERD and FD have a similar pathophysiologic mechanism, with delayed gastric emptying and visceral hypersensitivity [16, 17], which are more prevalent in women. However, IBS has a more complicated pathogenesis, including deregulation of brain-gut interaction and psychological disturbance [18].

Our results also supported the finding that overlapping GERD-FD had a more significant impact on quality of life than GERD did alone. Previous findings revealed the overlap of GERD with FGID had a statistically significant impact on SF-36 scores compared with GERD alone [7, 19, 20]. Among all GERD cases, patients with NERD were more sensitive to stimuli via visceral hypersensitivity, including not only acidic reflux, but also weakly acidic or gas reflux. The presence of FD features in GERD patients could aggravate symptoms resulting from the exposure of the esophageal mucosa to acid, with loss of this association in IBS features.

Our study had some limitations. Firstly, comorbidities in these patients that tend to influence the severity of GERD, such as chronic heart failure or chronic obstructive pulmonary disease, were not considered, and this might have led to inaccurate outcomes. Besides, our results simply related the impact of overlap FGID to the quality of life of GERD patients, so we did not provide data using multiple linear regression analysis. Secondly,

inadequate translation of the Chinese version of the symptom questionnaire (GERDQ) proposed by the Rome III criteria might have influenced the results of this study. Thirdly, not all of our patients with NERD were willing to undergo pH-metry monitoring, and this might have led to a misclassification of individuals with functional heartburn as NERD. Lastly, our study design was hospital based and included only a small number of cases. Further research that includes representative samples of the general population is needed to confirm these results.

## Conclusion

The results of our study showed high prevalence ratios of overlapping FGID, both FD and IBS, among GERD patients. The individuals with overlapping GERD and FD had lower quality of life scores than those with GERD alone.

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