

Overlap of Dyspepsia in Patients with Gastroesophageal Reflux Disease: Impact of Clinical, Metabolic, and Psychosocial Characteristics

Ching-Sheng Hsu^{1,2,3} · Shu-Hui Wen⁴ · Jui-Sheng Hung^{3,5} · Tso-Tsai Liu^{3,5} · Chih-Hsun Yi^{3,5} · Wei-Yi Lei^{3,5} · Fabio Pace⁶ · Chien-Lin Chen^{3,5}

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Abstract

Background Gastroesophageal reflux disease (GERD) and dyspepsia are highly prevalent in the general population with significant symptom overlap, while the interaction between both remains poorly understood.

Aim To examine whether GERD overlapping dyspepsia would have an impact on clinical and psychological features as compared with GERD alone.

Methods We performed a cross-sectional study in a GERD cohort ($n = 868$) that was previously recruited from a population-based GERD survey ($n = 2752$). We compared the clinical and psychological factors between patients with and without dyspeptic symptoms “epigastric pain or burning.” All participants were evaluated with Reflux

Disease Questionnaire score, Pittsburgh Sleep Quality Index score, Taiwanese Depression Questionnaire score, and State-Trait Anxiety Inventory score. Endoscopic findings were classified according to the Los Angeles classification.

Results Among the GERD population, 107 subjects had overlapping “epigastric pain or burning” (GERD-D), and 761 did not have these symptoms (GERD alone). GERD-D subjects had more severe GERD symptoms and were more often associated with irritable bowel syndrome (IBS) (OR 3.54, 95% CI 1.92–6.52) as compared subjects with GERD alone. In addition, GERD-D subjects had lower quality of sleep (OR 1.11, 95% CI 1.01–1.21), higher depression (OR 1.06, 95% CI 1.02–1.10), lower blood pressure (OR 0.45, 95% CI 0.22–0.95), and higher serum total cholesterol levels (OR 2.78, 95% CI 1.36–5.67) than GERD alone.

Conclusions GERD-D subjects are characterized with worsening clinical symptoms as well as higher

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✉ Chien-Lin Chen
harry.clchen@msa.hinet.net

Ching-Sheng Hsu
hsu.chingsheng@gmail.com

Shu-Hui Wen
shwen@mail.tcu.edu.tw

Jui-Sheng Hung
happyjohnhung@gmail.com

Tso-Tsai Liu
johoreboy@gmail.com

Chih-Hsun Yi
chihhsunyi@gmail.com

Wei-Yi Lei
aquarious@seed.net.tw

Fabio Pace
fabio.pace@unimi.it

- ¹ Division of Gastroenterology, Department of Internal Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taipei, Taiwan, ROC
- ² School of Post-Baccalaureate Chinese Medicine, Tzu Chi University, Hualien, Taiwan, ROC
- ³ School of Medicine, Tzu Chi University, Hualien, Taiwan, ROC
- ⁴ Department of Public Health, College of Medicine, Tzu Chi University, Hualien, Taiwan, ROC
- ⁵ Division of Gastroenterology, Department of Internal Medicine, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, No. 707, Sec. 3, Chung Yang Rd., Hualien 970, Taiwan, ROC
- ⁶ Division of Gastroenterology, Department of Internal Medicine, ASST Bergamo Est, “Bolognini” Hospital, Seriate, Italy

psychosocial, IBS, and metabolic comorbidities, but less erosive esophagitis. Our results indicate that clinical awareness of such overlapping condition would help optimize the management of GERD in clinical practice.

Keywords Dyspepsia · Cross-sectional study · Humans · Questionnaires

Abbreviations

GERD	Gastroesophageal reflux disease
IBS	Irritable bowel syndrome
MS	Metabolic syndrome
LA grade	Los Angeles classification system grade
RDQ	Reflux Disease Diagnostic Questionnaire
PSQI	Pittsburgh Sleep Quality Index score
TDQ	Taiwanese Depression Questionnaire score
STAI	State-Trait Anxiety Inventory score
WHR	Wait-to-hip ratio
BMI	Body mass index
EE	Erosive oesophagitis
IR	Insulin resistance
NSAIDs	Nonsteroidal anti-inflammatory drugs
PPIs	Proton pump inhibitors
H2RAs	Histamine-2 receptor antagonists
AC	Serum fasting blood glucose
HbA1c	Hemoglobin A1c
TG	Triglyceride
TC	Total cholesterol
LDL	Low-density lipoprotein
HDL	High-density lipoprotein
OR	Odds ratio
CI	Confidence interval
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

Introduction

Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal (GI) disorder with a huge economic burden worldwide, which significantly affects quality of life and increases the risk of esophageal adenocarcinoma [1–3]. It is prevalent in Asia and is currently estimated to affect more than 10% of the population [4–6]. Of note, the overlapping of GERD with other GI motility disorders is not uncommon. It was reported that 5–30% of community individuals with GERD had overlapping irritable bowel syndrome (IBS), and according to our previous survey, 10% of GERD individuals had overlapping IBS in Taiwan [7–10].

Functional dyspepsia (FD) is a condition characterized by chronic dyspeptic symptoms in the absence of other explainable conditions [11]. Because there exists a significant cultural difference in reporting of symptoms of

dyspepsia, and Asian patients appear to be bothered more by upper abdominal symptoms, bloating, and perceive less their abnormal bowel patterns [11], the Asian consensus report on FD has defined the dyspeptic symptoms in Asians as epigastric pain, epigastric burning, postprandial fullness, early satiation, bloating in the upper abdomen, nausea, vomiting and belching [11]. Although FD is also a common GI disorder in Asia with a reported prevalence of 8–23% [12–14] and overlap of FD with other functional bowel diseases such as GERD is common in Asia [15, 16], the interaction between FD and GERD remains poorly understood.

Identification of the cardinal manifestations of GERD is pivotal for the establishment of appropriate diagnostic approaches and treatment strategies [17] due to the symptom overlap. It may also help in understanding the pathophysiological mechanisms of FD and GERD [10]. We decided to perform a nested case–control study to examine the clinical characteristics, manifestations, and risk factors for GERD patients with or without overlapping dyspeptic symptoms. We focused on epigastric pain or burning, which are main dyspeptic symptoms in Asians [11]. We hypothesized that GERD overlapping “epigastric pain or burning” may have different manifestations compared to patients with GERD alone. We aimed to assess the presence of numerous clinical, metabolic, and psychological factors in GERD subjects with and without “epigastric pain or burning” and tried to identify which of these factors may be associated with a higher risk of “epigastric pain or burning” in a population of GERD patients.

Methods

Ethical Considerations

The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethical Committee of Taipei and Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation. Written informed consent was obtained from each participant.

Study Population

In a previous prospective study of clinical, metabolic, and psychological characteristics in patients with gastroesophageal reflux disease, a total of 2752 adult subjects who had undergone voluntary endoscopy in health examinations were enrolled from the Health Management Center of Taipei and Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation during March 2012 to August 2013 as previously reported [7]. In brief, all study participants completed questionnaires including Reflux Disease

Questionnaire (RDQ) score [18, 19], Rome III Diagnostic Questionnaires [20], Pittsburgh Sleep Quality Index (PSQI) score [21], Taiwanese Depression Questionnaire (TDQ) score [22], State-Trait Anxiety Inventory (STAI) score [23], and received standardized sedated upper GI endoscopy. Erosive esophagitis (EE) was graded from A to D according to the Los Angeles classification system using standard comparator photos. Upper GI endoscopy was done by experienced endoscopists who were blinded to the results of the questionnaire. Any discordance in diagnosis was discussed by at least three experienced endoscopists, and the final diagnosis was made by consensus [7, 24, 25].

The RDQ is a self-administered questionnaire that examines symptoms of heartburn, acid regurgitation, and dyspepsia [18]. It includes 12 questions measuring the frequency, severity, and duration of the following symptoms: (1) acid taste in the mouth and movement of materials upwards from the stomach (Regurgitation scale); (2) pain or burning behind the breastbone (Heartburn scale); and (3) pain or burning in the upper stomach (Dyspepsia scale) [26]. Most response options are scaled with categories ranging from 0 to 5 points. Any individual who has a RDQ score ≥ 3 in non-dyspepsia scales is defined as having troublesome reflux symptoms, and individuals who have a score ≥ 3 in dyspepsia scale are defined as having “epigastric pain or burning” (dyspepsia) [26].

We defined GERD patients as individuals who had a diagnosis of endoscopic LA grade $\geq A$ or troublesome reflux symptoms, and GERD patients with overlapping “epigastric pain or burning” as individuals had a diagnosis of both GERD and “epigastric pain or burning” (GERD-D). Further inclusion criteria were (1) absence of any gastrointestinal surgery, liver cirrhosis, or malignancy, (2) absence of having proton pump inhibitors (PPIs), histamine-2 receptor antagonists (H2RAs), aspirin, or NSAIDs in the 6 months preceding the invitation, and (3) complete questionnaire data [27]. Subjects who were not GERD patients or with incomplete data were excluded. Finally, a total of 868 GERD subjects were enrolled in the present study, including patients with GERD alone ($n = 761$) and GERD overlapping “epigastric pain or burning” (GERD-D; $n = 107$; Fig. 1).

Demographic, Serological, Biochemical Data, and Medical Information

Demographic, serological, biochemical, as well as medical information of all participants were recorded. Blood samples were collected in the morning after a 12-h fast and measured by standard laboratory techniques.

Metabolic syndrome was defined based on the National Cholesterol Education Program (NCEP) Adult Treatment

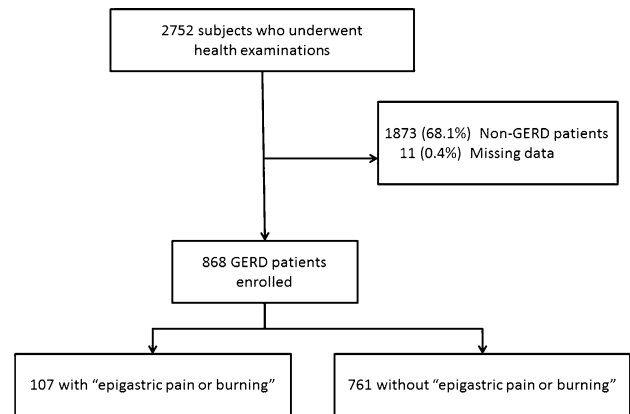


Fig. 1 Flow of subjects in the study

Panel III (ATPIII) definition as the presence of at least three of the following five characteristics: the presence of abdominal obesity (a waist circumference ≥ 90 cm for Taiwanese men and ≥ 80 cm for Taiwanese women); TG concentration ≥ 150 mg/dL; HDL-cholesterol concentration < 40 mg/dL in men and < 50 mg/dL in women; blood pressure $\geq 130/\geq 85$ mmHg; or fasting plasma glucose ≥ 100 mg/dL [28].

Medical information included smoking, alcohol consumption, coffee consumption, black or green tea intake, history of diabetes mellitus, hypertension, and hyperlipidemia, and use of the following medications: aspirin, NSAIDs, H2RAs, or PPIs [7, 27]. Categorical variables of coffee consumption (yes or no), black or green tea intake (yes or no), current smoker (yes or no), and alcohol consumption (yes or no) were created for analyses [29].

Questionnaire

The Rome III Diagnostic Questionnaire is used for the diagnosis of IBS to examine the frequency and onset of recurrent abdominal pain or discomfort with two or more of the following changes, including pain/discomfort relieved by a bowel movement, onset of pain/discomfort related to a change in frequency of stool or the appearance of stool [20]. All subjects had colonoscopy at the time of enrollment to exclude structural disorders.

The PSQI is an effective instrument used to measure the quality and patterns of sleep over the last month. Scoring of the answers is based on a 0–3 scale, and a global sum ≥ 5 indicates a poor sleep [21].

The TDQ, which is a four-point scale with 18 items, is a culturally specific depression self-rating instrument for effective screening of depression and has satisfactory reliability and validity [22]. Subjects are guided to rate each item on a scale from 0 to 3. TDQ scores range from 0 to 54.

The STAI is a commonly used measure of trait and state anxiety [23]. It can be used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. It has 20 items for assessing trait anxiety (T-anxiety) and 20 for state anxiety (S-anxiety). All items are rated on a four-point scale (e.g., from “Almost Never” to “Almost Always”). Higher scores indicate greater anxiety. The STAI is appropriate for those who have at least a sixth-grade reading level.

Statistical Analysis

Except descriptive statistics (frequencies, percentages, means, and standard deviations), Chi-square test, and independent-sample *t* test were used to analyze categorical and continuous variables, respectively. A multivariate logistic regression model was performed to assess associating factors of “epigastric pain or burning” to estimate adjusted odds ratios (OR) and 95% confidence intervals (CI) of these factors. We used full model by using the “epigastric pain or burning” as dependent variable, and age, sex, education, income, BMI, coffee consumption, tea intake, alcohol consumption, smoking status, RDQ score, PSQI score, TDQ score, STAI score, *Helicobacter pylori* infection, metabolic syndrome, history of IBS, hypertension, diabetes mellitus, and hyperlipidemia as independent variables. A stratified analysis looking at those who had esophagitis was also performed. SAS Version 9.2 (SAS Institute, Cary, NC, USA) was used for all analyses. Statistical significance was set as a *P* value of <0.05.

Results

Demographic Characteristics of the Study Sample

Among the study population, 268 had troublesome reflux symptoms as identified by the RDQ ≥ 3 in non-dyspepsia scales, 107 had “epigastric pain or burning” as identified by a RDQ score ≥ 3 in dyspepsia scale (GERD-D), and 733 had a diagnosis of endoscopic LA grade $\geq A$ (EE). In total, 107 subjects had GERD-D and 761 subjects had GERD alone were included in our analyses. Demographic and psychological factors of these study populations are listed in Table 1. There was no significant difference between these two study groups in factors of age, gender, education, waist-to-hip ratio, income, coffee consumption, tea intake, alcohol consumption, and tobacco use. However, GERD-D subjects had lower BMI ($P = 0.02$) and higher RDQ score (P value <0.001) that means GERD-D subjects were thinner and had more severe GERD symptoms. Among psychological factors, GERD-D subjects had higher PSQI score ($P < 0.001$), higher TDQ score

($P < 0.001$), and higher STAI score ($P < 0.001$). Therefore, GERD-D subjects seem to have lower quality of sleep, higher depression, and anxiety scores than subjects with GERD alone.

Comorbidities in the GERD Subjects with “Epigastric Pain or Burning”

To identify factors associated with “epigastric pain or burning” in GERD, we examined the differences in the distribution of comorbidities between GERD subjects with and without “epigastric pain or burning.” Table 2 shows the comparison of endoscopic findings, metabolic characters, and other comorbidities between subjects with GERD-D and GERD alone. We found that GERD-D subjects were less associated with erosive reflux disease ($P < 0.001$), more frequently consulted healthcare providers for IBS ($P < 0.001$), but less frequently consulted healthcare providers for hypertension ($P = 0.027$) as compared to subjects with GERD alone. Moreover, GERD-D subjects had lower systolic blood pressure ($P = 0.045$), diastolic blood pressure ($P = 0.011$), and higher serum total cholesterol levels than GERD alone ($P = 0.021$).

Multivariate Analyses

Compared with GERD alone subjects, GERD-D patients had higher PSQI score (adjusted OR 1.11, 95% CI 1.01–1.21), higher TDQ score (adjusted OR 1.06, 95% CI 1.02–1.10), and were more frequently co-occurring with IBS (adjusted OR 3.54, 95% CI 1.92–6.52), and associated with hyperlipidemia (adjusted OR 2.78, 95% CI 1.36–5.67), but less frequently with hypertension (adjusted OR 0.45, 95% CI 0.22–0.95) after adjusting for clinical, metabolic, and psychosocial characteristics (Table 3). In the subgroup analysis among 733 EE patients, GERD-D subjects had higher TDQ score (adjusted OR 1.06, 95% CI 1.01–1.11) and were more frequently co-occurring with IBS (adjusted OR 6.18, 95% CI 2.80–13.65), associated with *H. pylori* infection (adjusted OR 2.16, 95% CI 1.11–4.22) and hyperlipidemia (adjusted OR 2.66, 95% CI 1.11–6.36), but less frequently with hypertension (adjusted OR 0.25, 95% CI 0.09–0.69) than GERD alone subjects (Supplementary Table 1).

Discussion

In this study, we found that an overlap of GERD and “epigastric pain or burning” is not uncommon in Taiwan, with a prevalence of 12.3% in a general population-based GERD sample. We also demonstrated different clinical and psychological profiles between patients with GERD alone

Table 1 Demographic and psychological factors of patients with GERD and dyspepsia overlap with GERD

Characteristics	GERD only (<i>n</i> = 761)	GERD-D (<i>n</i> = 107)	<i>P</i> value
<i>Demographic factors</i>			
Male, <i>n</i> (%)	473 (62.16)	57 (53.27)	0.078
Age (years)	53.06 ± 11.61	50.77 ± 10.55	0.055
<50	275 (36.14)	50 (46.73)	0.100
50–60	278 (36.53)	34 (31.78)	
>60	208 (27.33)	23 (21.50)	
BMI (kg/m ²)	24.84 ± 3.87	23.91 ± 3.67	0.020*
<24	329 (43.23)	59 (55.14)	0.051
24–27	243 (31.93)	30 (28.04)	
≥27	189 (24.84)	18 (16.82)	
WHR	0.90 ± 0.08	0.89 ± 0.08	0.416
Education, <i>n</i> (%) (years)			0.149
≤ 9	207 (27.20)	21 (19.63)	
10–12	233 (30.62)	41 (38.32)	
≥ 12	321 (42.18)	45 (42.06)	
Income, <i>n</i> (%)			0.911
Enough	417 (54.80)	59 (55.14)	
Rich	293 (38.50)	42 (39.25)	
Poor	51 (6.70)	6 (5.61)	
Coffee	430 (56.58)	61 (57.01)	0.933
Tea	455 (60.26)	69 (64.49)	0.403
Alcohol	318 (41.84)	42 (39.62)	0.664
Smoke	103 (13.55)	16 (14.95)	0.693
RDQ score	3.11 ± 4.73	11.47 ± 7.33	<0.001*
<i>Psychological factors</i>			
PSQI score	5.42 ± 2.48	7.02 ± 3.21	<0.001*
TDQ score	7.52 ± 6.96	14.00 ± 10.32	<0.001*
STAI score	37.99 ± 8.31	41.42 ± 8.66	<0.001*

Data are shown by mean ± SD or proportion of the character

A GERD subject was defined as any individual who has a diagnosis of endoscopic LA grade ≥ A or RDQ score ≥ 3 (please see the text for the detailed information)

* *P* < 0.05 is considered as statistical significance

and symptom overlap of GERD and “epigastric pain or burning.” GERD patients with concomitant “epigastric pain or burning” are associated with more severe GERD symptoms, poor sleep quality, greater depression and anxiety, and have more frequently co-occurring with IBS and hyperlipidemia, but less frequently with hypertension. From these data, it appears that the primary risks of symptom overlap between GERD and “epigastric pain or burning” patients pertain to greater psychological distress such as sleep disturbance, depression, anxiety, and comorbidity. Awareness of identifying and resolving these associated manifestations in GERD patients may markedly improve the outcome in the management of GERD patients.

First, we identified GERD symptoms, sleep quality and patterns, depression and anxiety as risk factors for “epigastric pain or burning” in GERD patients. Our study

echoed previous study that demonstrated an increased risk of anxiety and lower health-related quality of life in patients with FD. However, because functional gastrointestinal and motility disorders are known as multifactorial illnesses with overlapping in a variable combination of genetic factors, gut infections, brain–gut interactions, and psychological disturbance interacting simultaneously [17, 30–33], all these factors are risk factors for the development of both “epigastric pain or burning” and GERD [17, 30, 34] and cannot fully explain the increased risk of dyspepsia in GERD subjects. Thus, it may be that there are specific factors, which may actually be promoting the occurrence of “epigastric pain or burning” in the GERD population. As Asian patients appear to be bothered more by upper abdominal symptoms, bloating, and perceive less their abnormal bowel patterns [11, 30, 35, 36], the prevalence of coexistence in GERD and “epigastric

Table 2 Endoscopic findings, medical history, and metabolic syndrome of patients with GERD only, dyspepsia overlap with GERD

Characteristics	GERD only (<i>n</i> = 761)	GERD-D (<i>n</i> = 107)	<i>P</i> value
Endoscopic findings			
Erosive esophagitis, <i>n</i> (%)	663 (87.12)	70 (65.42)	<0.001*
<i>H. pylori</i> infection	160 (21.11)	24 (22.43)	0.755
Medical history			
IBS	51 (6.70)	31 (28.97)	<0.001*
Hypertension	173 (23.90)	14 (14.00)	0.027*
Diabetes	62 (8.56)	7 (7.00)	0.597
Hyperlipidemia	86 (11.88)	18 (18.00)	0.084
Metabolic syndrome			
Waist circumference	86.67 ± 10.63	84.81 ± 10.13	0.089
Systolic blood pressure (mmHg)	121.9 ± 15.71	118.5 ± 16.95	0.045*
Diastolic blood pressure (mmHg)	76.39 ± 11.85	73.18 ± 12.01	0.011*
Fasting blood glucose (mg/dL)	98.61 ± 23.61	95.88 ± 17.16	0.148
Total cholesterol (mg/dL)	188.2 ± 38.20	199.7 ± 48.17	0.021*
Triglyceride (mg/dL)	127.0 ± 85.23	133.6 ± 87.87	0.464
HDL (mg/dL)	48.52 ± 14.35	49.80 ± 12.74	0.392
Metabolic syndrome	243 (31.93)	31 (28.97)	0.537

Data are shown by mean ± SD or proportion of the character

A GERD subject was defined as any individual who has a diagnosis of endoscopic LA grade \geq A or RDQ score \geq 3 (please see the text for the detailed information)

* *P* < 0.05 is considered as statistical significance

pain or burning” in this study may be partly explained by the socioeconomic and cultural features in Asian [34]. Of note, a proportion of patients with overlap of “epigastric pain or burning” and GERD have more frequent consultation for IBS, implying the existence of a subgroup with more severe symptoms that may affect pan-gastrointestinal tract motility.

Interestingly, we also demonstrated that “epigastric pain or burning” was more frequently co-occurring with hyperlipidemia, but less frequently with hypertension. Because patients using lipid-lowering agents frequently complain of dyspepsia [37] and since both hypertension and cardiovascular diseases have been physiopathologically linked to reflux esophagitis and Barrett’s esophagus [38], our findings are not surprising and seem to confirm previous studies. However, to further elucidate the underlying mechanisms, future investigations on factors that are known to increase blood pressure or cause hyperlipidemia, such as insulin resistance, high fat and salt intake, sedentary lifestyle, stress and genetic factors in GERD-D subjects, are needed. In addition, although alcohol intake per se may worsen dyspeptic symptoms, the association of alcohol consumption and risks of esophageal disorders or dyspepsia seems dependent on the amount and the age of alcohol consumption [39, 40]. Therefore, we only identified a marginal significant association between alcohol consumption and GERD-D (OR 0.6, 95% CI 0.34–1.04, *P* = 0.068). Although *H. pylori* may worsen dyspeptic symptoms, as patients with EE have a lower *H. pylori*

infection rate in Taiwan [27], a higher *H. pylori* infection rate in non-EE subjects may weaken the pathogenic effect of *H. pylori* on dyspeptic symptoms. Therefore, we identified an association between *H. pylori* infection and dyspeptic symptoms in EE subjects, not in non-EE subjects.

This study has a number of inherent limitations that warrant mention. First, because this study was cross-sectional, only associations could be determined. However, our findings may serve as a hypothesis forming guide for developing future prospective trials, and studies with a longitudinal design and paired controls to elucidate possible causal relationships of clinical and psychological characters between GERD with and without “epigastric pain or burning” are ongoing. Second, as most of the participants enrolled from health examinations were generally healthy, the severity of esophagitis among these subjects was mild [4, 7]. Further studies to examine the relationship between GERD and “epigastric pain or burning” among subjects with different severity of esophagitis or different races or cultures are necessary. Third, as most Asian patients with dyspepsia have PDS-type (i.e., bloating/discomfort) rather than EPS-type (epigastric pain) FD, our study may probably underestimate the true overlap between FD/GERD overlap. We used the dyspepsia scale in RDQ to define a diagnosis of “epigastric pain or burning,” recall bias for the questionnaire should be considered in the interpretation of our findings. A different definition for dyspepsia, such as the Rome III criteria, should be examined in future studies. Moreover, self-reported data

Table 3 Multivariate logistic regression analyses of factors associated with dyspepsia in the GERD sample

Characteristics	OR (95% CI)	P value
Female, male = ref.	0.98 (0.58–1.67)	0.944
Age, <50 years = ref.		
50–60 years	0.76 (0.42–1.39)	0.597
>60 years	0.77 (0.37–1.61)	0.707
Education, ≤9 years = ref.		
10–12 years	1.66 (0.82–3.36)	0.107
≥12 years	1.18 (0.55–2.53)	0.766
Income, poor = ref.		
Enough	1.17 (0.41–3.34)	0.916
Rich	1.47 (0.50–4.38)	0.372
BMI, <24 = ref.		
24–27	0.73 (0.41–1.31)	0.919
≥27	0.56 (0.28–1.14)	0.206
Coffee consumption	0.87 (0.53–1.44)	0.586
Tea intake	1.25 (0.74–2.11)	0.404
Alcohol consumption	0.60 (0.34–1.04)	0.068
Smoking status	1.05 (0.51–2.18)	0.891
PSQI score	1.11 (1.01–1.21)	0.029*
TDQ score	1.06 (1.02–1.10)	0.005*
STAI score	0.99 (0.95–1.03)	0.619
<i>H. pylori</i> infection	1.29 (0.73–2.30)	0.382
Metabolic syndrome	1.22 (0.68–2.19)	0.513
IBS	3.54 (1.92–6.52)	<0.001*
Hypertension	0.45 (0.22–0.95)	0.035*
Diabetes mellitus	0.81 (0.30–2.23)	0.687
Hyperlipidemia	2.78 (1.36–5.67)	0.005*

Multivariate logistic regression model was used. Use the dyspepsia as dependent variable, and age, sex, education, income, BMI, coffee consumption, tea intake, alcohol consumption, smoking status, RDQ score, PSQI score, TDQ score, STAI score, *H. pylori* infection, metabolic syndrome, history of IBS, hypertension, diabetes mellitus, and hyperlipidemia as independent variables. Reference group (ref.) means that category served as the reference group for calculating an odds ratio

* $P < 0.05$ is considered as statistical significance

were used to exclude subjects who had taken a PPI or H2RAs in the previous 6 months, and incorrect reports may weaken the observed association. Lastly, we only focused on clinical characteristics about GERD, “epigastric pain or burning,” and EE in this study. As different dimensions in quality of life and physiological effects may affect the symptoms of GERD and FD, further evaluation with various dimensions in quality of life and physiological tests will be more informative.

In summary, our data demonstrate significantly clinical and psychological differences in GERD patients with and without concurrent “epigastric pain or burning.” GERD subjects overlapping with “epigastric pain or burning” are more likely to have severe reflux symptoms, frequent IBS-

related consultation behavior, greater depression, anxiety and poorer sleep quality than those with GERD alone. It is, therefore, important to be aware that both concurrent dyspeptic symptoms and psychological distress can contribute to worsening symptoms of GERD. Whether these associations imply a direct pathophysiological interaction between dyspepsia and GERD awaits further investigation.

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Authors' contributions C-LC was involved in study concept and design. J-SH, T-TL, C-HY, W-YL, and C-LC were involved in acquisition of data. C-SH, S-HW, J-SH, and C-LC were involved in analysis and interpretation of data. C-SH, S-HW, J-SH, and C-LC drafted the manuscript. C-SH, S-HW, FP, and C-LC were involved in critical revision of the manuscript for important intellectual content. S-HW was involved in statistical analysis. C-SH and C-LC obtained the funding. C-SH, S-HW, and C-LC were involved in administrative, technical, or material support. C-LC was involved in study supervision.

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Compliance with ethical standards

Conflict of interest All authors declare no other potential conflicts (financial, professional, or personal) that are relevant to the manuscript.

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