

Gastrointestinal symptoms and associated factors in Chinese patients with functional dyspepsia

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gastroenterology in Wuhan, Beijing, Shanghai, Guangzhou, and Xi'an, China were referred for this study. All of the patients fulfilled the Rome III criteria for FD. Baseline demographic data, dyspepsia symptoms, anxiety, depression, sleep disorder, and drug treatment were assessed using self-report questionnaires. Patients completed questionnaires at baseline and after 1, 3, 6 and 12 mo follow-up. Comparison of dyspepsia symptoms between baseline and after follow-up was explored using multivariate analysis of variance of repeated measuring. Multiple linear regression was done to examine factors associated with outcome, both longitudinally and horizontally.

RESULTS: Nine hundred and forty-three patients (89.9% of the original population) completed all four follow-ups. The average duration of follow-up was 12.24 ± 0.59 mo. During 1-year follow-up, the mean dyspeptic symptom score (DSS) in FD patients showed a significant gradually reduced trend ($P < 0.001$), and similar differences were found for all individual symptoms ($P < 0.001$). Multiple linear regression analysis showed that sex ($P < 0.001$), anxiety ($P = 0.018$), sleep disorder at 1-year follow-up ($P = 0.019$), weight loss ($P < 0.001$), consulting a physician ($P < 0.001$), and prokinetic use during 1-year follow-up ($P = 0.035$) were horizontally associated with DSS at 1-year follow-up. No relationship was found longitudinally between DSS at 1-year follow-up and patient characteristics at baseline.

CONCLUSION: Female sex, anxiety, and sleep disorder, weight loss, consulting a physician and prokinetic use during 1-year follow-up were associated with outcome of FD.

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Key words: Functional dyspepsia; Gastrointestinal symptoms; Dyspeptic symptom score; *Helicobacter pylori*

Abstract

AIM: To study the evolution of gastrointestinal symptoms and associated factors in Chinese patients with functional dyspepsia (FD).

METHODS: From June 2008 to November 2009, a total of 1049 patients with FD (65.3% female, mean age 42.80 ± 11.64 years) who visited the departments of

lori infection; Postprandial distress syndrome; Epigastric pain syndrome; Rome III criteria

Core tip: This is a prospective study with Chinese patients to explore the clinical course of functional dyspepsia (FD), and evaluate the potential risk factors associated with it, using the Rome III criteria both longitudinally and horizontally. The sample size in this study was large and there was a good response rate. The mean dyspepsia symptom score for both total and individual symptoms showed a significant gradually reduced trend. Female sex, anxiety, and sleep disorder, weight loss, consulting a physician and prokinetic use during 1-year follow-up were associated with the outcome of FD.

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INTRODUCTION

Functional dyspepsia (FD) is a highly prevalent gastrointestinal disorder that is defined by the presence of symptoms thought to originate in the gastroduodenal region, without identifiable cause and diagnosed by routine tests^[1,2]. According to the Rome III criteria, patients are classified as postprandial distress syndrome (PDS) or epigastric pain syndrome (EPS) based upon the predominant symptom (*i.e.*, postprandial fullness, early satiation, or epigastric pain, and burning)^[1]. The reported prevalence of FD symptoms varies between 19% and 41%^[3]. FD has a significant impact on quality of life and imposes a substantial economic burden on society due to costs of physician visits, medication, and absenteeism^[3,4].

The course of FD is always chronic, with a relapsing-remitting pattern, and has been poorly studied^[5]. In spite of the prevalence of FD being stable over time, the reverse in symptom status is high^[6]. Many studies have reported that a significant number of patients with FD improve or become asymptomatic over time, suggesting that a proportion of patients go into symptom remission, but the rates of symptom disappearance varies widely^[5,7].

The pathophysiology of FD also remains poorly understood and is likely to be multifactorial^[8]. Many pathogenic factors have been proposed for FD including genetic, environmental, pathological, and psychological factors^[9]. Psychosocial factors such as depression, anxiety and stressful life events (*e.g.*, history of abuse) are considered to play a role in the development of FD^[10,11]. A relationship between *Helicobacter pylori* (*H. pylori*) infection and FD has also been reported^[12]. Similarly, several

studies have demonstrated that sleep disorder is associated with functional gastrointestinal disorders such as irritable bowel syndrome, gastroesophageal reflux disease, and FD^[13-15]. Nevertheless, it is not clear whether such pathogenic factors affect the clinical course of FD.

Accordingly, this longitudinal study followed up a group of Chinese patients with FD over 1 year. We aimed to explore the evolution of FD symptoms, and evaluate the potential risk factors both longitudinally and horizontally.

MATERIALS AND METHODS

Patient selection

A total of 1049 patients with FD (364 male and 685 female, aged 20-79 years, mean 42.80 ± 11.64 years) who fulfilled the Rome III criteria were enrolled. These were outpatients who visited departments of gastroenterology in five cities in China (Wuhan, Beijing, Shanghai, Guangzhou, and Xi'an) from June 2008 to November 2009.

The patients had one or more dyspeptic symptoms, including troublesome postprandial fullness, early satiation, epigastric pain, or epigastric burning for the past 3 mo, with symptom onset at least 6 mo before diagnosis. All of the FD patients had undergone upper gastrointestinal endoscopy, abdominal ultrasound, and/or barium meal X-ray examination in a tertiary hospital. In all cases, there was no evidence of organic, systemic, or metabolic disease that was likely to explain the symptoms.

Patients were excluded if they: (1) had upper gastrointestinal organic diseases such as esophagitis, peptic ulcer, or peptic neoplasm that were found by gastroscopy or barium meal X-ray examination and abdomen ultrasonography; (2) had chronic diseases such as diabetes mellitus, hyperthyroidism, scleroderma, chronic renal failure, or congestive heart failure; (3) had a history of abdominal surgery; or (4) were pregnant or preparing to conceive a child, or lactating during the study period.

Data collection and synthesis

Baseline data: All 1049 FD patients were asked to finish a self-report questionnaire face to face. To ensure content validity and usability, physicians were trained initially to give instructions to patients and did not intervene with the patients' medical management.

The baseline self-reported questionnaire included several clinical variables involving demographics (age, sex, height, weight, and marital status), tobacco and alcohol use, educational level, economic situation, life satisfaction, physical labor, *H. pylori* status, severity and frequency of each dyspepsia symptom, bowel symptom comorbidity, psychosocial factors (anxiety and depression), sleep disorder, major mental stimulation, history of abuse and drug treatment (prokinetics, gastric mucosa protectants, antacids, anti-*H. pylori* therapy, and traditional Chinese medicine). The data for dyspepsia and bowel symptoms were collected using a Chinese version of the

validated Rome III diagnostic questionnaire for adult functional gastrointestinal disease^[16]. This questionnaire has been repeatedly tested and carefully validated^[17].

Follow-up data: FD patients were asked to visit the department of gastroenterology to finish a follow-up questionnaire at 1, 3, 6 and 12 mo after the first visit. The follow-up questionnaire was the same as the baseline questionnaire, but did not include some details such as sex, educational level, economic situation, life satisfaction, physical labor, major mental stimulation, and history of abuse.

Diagnosis of *H. pylori* infection

At upper gastrointestinal endoscopy, biopsies were acquired and processed for rapid urease test. A ¹³C/¹⁴C-urea breath test was also used to assess *H. pylori* status.

Definition of body mass index

Body mass index (BMI) was calculated and categorized as weight (kg)/height (m²) according to World Health Organization recommendations.

Economic situation

Economic situation was classified as rich, sufficient, well-off and poor according to the expending percentage for food in whole income as < 1/5, < 1/3, 1/2, and > 1/2.

Educational level

Educational level was divided into seven: illiteracy, elementary school, junior high school, high school, junior college, university, and graduate and above. If the patients were illiterate or had finished elementary school education, they were judged as having a low level of education. If the patients had completed junior high school or high school education, they were regarded as having a medium level of education. Patients who had completed junior college education or above were considered to have a high level of education.

Tobacco and alcohol use

Current smokers were defined as individuals smoking cigarettes and having no other former tobacco use. Alcohol use was defined as consumption of > 100 g/wk alcohol.

Assessment of dyspeptic symptoms

Dyspeptic symptoms that were recorded and assessed included postprandial fullness, early satiation, epigastric pain, epigastric burning, belching, nausea, vomiting, and bloating. Each symptom was graded and scored on a Likert scale according to its severity as follows: 0, absent; 1, mild (not influencing daily activities); 2, relevant (diverting from but not urging modifications in daily activities); and 3, severe (influencing daily activities markedly enough to urge modifications). Frequency of each symptom was also graded as follows: 1, occurring < 1 d/mo; 2, occur-

ring 1 d/mo; 3, occurring 2-3 d/mo; 4, occurring 1 d/wk; 5, occurring > 1 d/wk; and 6, occurring every day. The score for a single dyspeptic symptom was an aggregate of frequency and severity ratings, ranging from 0 to 9. Dyspeptic symptoms score (DSS) was assessed by summing the score of eight dyspepsia symptoms.

Psychosocial factors (anxiety and depression) and sleep disorder

The questionnaires used for assessment of psychological factors and sleep disorder were established according to a Chinese version of the Validated Rome III Psychosocial Alarm Questionnaire for functional gastrointestinal disease^[16,18]. In previous studies these questionnaires have been used to assess the psychological factors and sleep status of Chinese patients^[19].

For problems related to anxiety and depression in the past 3 mo, the patients answered the question: Did you feel nervous irritable or depressed (yes/no)? If patients chose yes, they had to answer the next question about how often they felt nervous irritable or depressed: 1, occasionally; 2, sometimes; 3, frequently; 4, most of the time. Patients felt nervous irritable or depressed frequently or most of the time, indicating that anxiety or depression was present^[16]. In the present study, we judged "nervous irritability" or "depression" occurring frequently or most of the time as "anxiety state" or "depression state".

Subjective sleep disorder in patients was measured with one question (yes/no). Symptoms of sleep disorder included trouble falling asleep, shallow sleep/dreaminess, sleep time < 6 h, early morning awakening, and daytime sleepiness.

History of abuse

A history of abuse in patients was measured with a question as follows: Have you ever been abused (yes/no)? If patients chose yes, they stated whether the abuse was physical or mental.

Statistical analysis

All statistical analyses were assessed using SPSS for Windows version 13. A two-sided *P* value < 0.05 was regarded as statistically significant. Data are presented as mean ± SD. To assess whether those who completed all four follow-ups were representative of the original study population, we compared the baseline characteristics between the follow-up population and those who were lost to follow-up, using Pearson's χ^2 test (categorical variables), Mann-Whitney *U* test (ordinal variables, such as BMI) and *t* test (continuous variables). Comparison between all individual dyspepsia symptoms at initial visit and at the four follow-ups was explored using multivariate analysis of variance (MANOVA) of repeated measuring. Univariate association measures between patient characteristics (baseline as well as 1-year follow-up) and DSS at 1-year follow-up were calculated using Pearson's

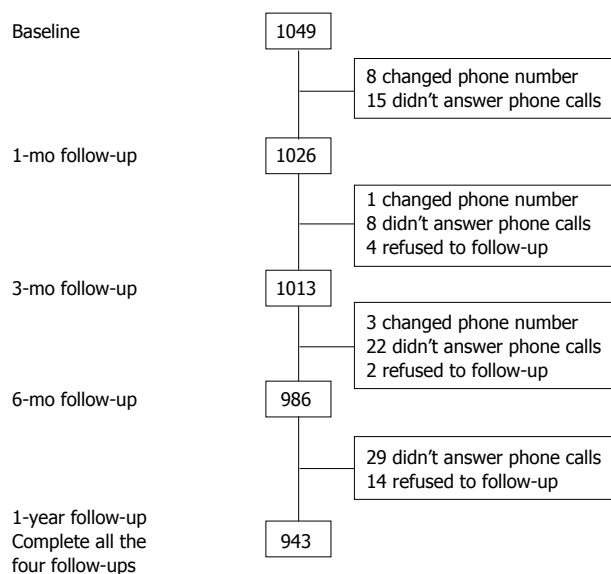


Figure 1 Flowchart of study participants.

s correlation and non-parametric one-way ANOVA. Risk factors associated with DSS at final follow-up, both longitudinally and horizontally, were determined by performing multiple linear regressions.

RESULTS

Patient characteristics and response rate

Of the 1049 FD patients originally enrolled, 1026 patients (97.8% of the baseline sample) completed the 1-mo study; 1013 patients (96.6% of the baseline sample) completed the 3-mo study; 986 patients (94.0% of the baseline sample) completed the 6-mo study; and 943 patients (89.9% of the baseline sample) completed the 1-year study (Figure 1).

The 943 patients who completed the baseline and all four follow-up questionnaires were included in this study. The average duration of follow-up was 12.24 ± 0.59 mo. The mean age of the follow-up population was 42.99 ± 11.74 years, and 603 (63.9%) were female; 176 (18.7%) had bowel symptom comorbidity, and 230 (24.4%) were positive for *H. pylori*. Men, alcohol users, those with higher educational level and better economic situation, and those who had consulted a physician were significantly more likely to be successfully followed up ($P < 0.05$ for all analyses) (Table 1).

Comparison of dyspepsia symptoms between baseline and at follow-up

The mean DSS in FD patients at baseline, and 1, 3 and 6 mo and 1 year follow-up was 22.05 ± 9.89 , 14.04 ± 9.38 , 12.05 ± 9.09 , 10.08 ± 8.89 and 8.97 ± 8.62 , respectively. This means that during 1 year follow-up, the mean DSS in FD patients showed a significant gradually reduced trend and all pairwise comparisons were statistically significant (all $P < 0.001$).

Table 1 Demographics and baseline characteristics of patients who completed all four follow-ups compared with those who were lost to follow-up

Characteristic	Complete all four follow-ups (n = 943)	Lost to follow-up (n = 106)	P value
Sex (female)	603 (63.9)	82 (77.4)	0.006
Smoker	202 (21.4)	16 (15.1)	0.128
Alcohol user	278 (29.5)	15 (14.2)	0.001
Marital status (married)	815 (86.4)	95 (89.6)	0.357
Physical labor			0.537
High	34 (3.6)	3 (2.8)	
Medium	238 (25.2)	31 (29.2)	
Low	671 (71.2)	72 (67.9)	
Life satisfaction			0.292
High	171 (18.1)	13 (12.3)	
Medium	732 (77.6)	90 (84.9)	
Low	40 (4.2)	3 (2.8)	
Educational level			0.011
High	336 (35.6)	28 (26.4)	
Medium	455 (48.3)	51 (48.1)	
Low	152 (16.1)	27 (25.5)	
Economic situation			0.03
Rich	40 (4.2)	3 (2.8)	
Sufficient	405 (42.9)	34 (32.1)	
Well-off	469 (49.7)	67 (63.2)	
Poor	29 (3.1)	2 (1.9)	
BMI (kg/m ²)			0.071
Obesity	138 (14.6)	10 (9.4)	
Normal	709 (75.2)	81 (76.4)	
Thin	96 (10.2)	15 (14.2)	
Bowel symptom	176 (18.7)	23 (21.7)	0.45
<i>H. pylori</i> status (positive)	230 (24.4)	22 (20.8)	0.14
Consulting a physician	908 (96.3)	91 (85.8)	< 0.001
Mean age (yr)	42.99 ± 11.74	41.11 ± 10.65	0.116
DSS	22.05 ± 9.89	20.25 ± 10.77	0.079

Data are expressed as absolute numbers (percentage) or mean \pm SD. Significant variables in italic/bold ($P < 0.05$); BMI: Body mass index calculated; *H. pylori*: *Helicobacter pylori*; DSS: Dyspeptic symptom score.

Similar differences were observed for all individual symptoms (Figure 2). The mean symptom scores for both postprandial fullness and belching during 1 year follow-up showed a significant reduced trend and all pairwise comparisons were statistically significant (all $P < 0.001$).

The mean symptom scores for early satiation, nausea and bloating during 1 year follow-up decreased significantly and all pairwise comparisons were statistically different (all $P < 0.001$, except for the difference between 3 and 6 mo follow-up, $P = 0.037$, $P = 0.035$, $P = 0.102$, and the difference between 6 mo and 1 year follow-up, $P = 0.333$, $P = 0.034$, $P = 0.213$).

There was a marked decreased trend in mean symptom scores for both epigastric pain and epigastric burning during 1-year follow-up, and there were significant differences in all pairwise comparisons (all $P < 0.001$, except for the difference between 6 mo and 1 year follow-up, $P = 0.401$, $P = 0.028$).

The mean symptom scores for vomiting was reduced markedly, with all pairwise comparisons showing a significant difference (all $P < 0.001$, except for the difference

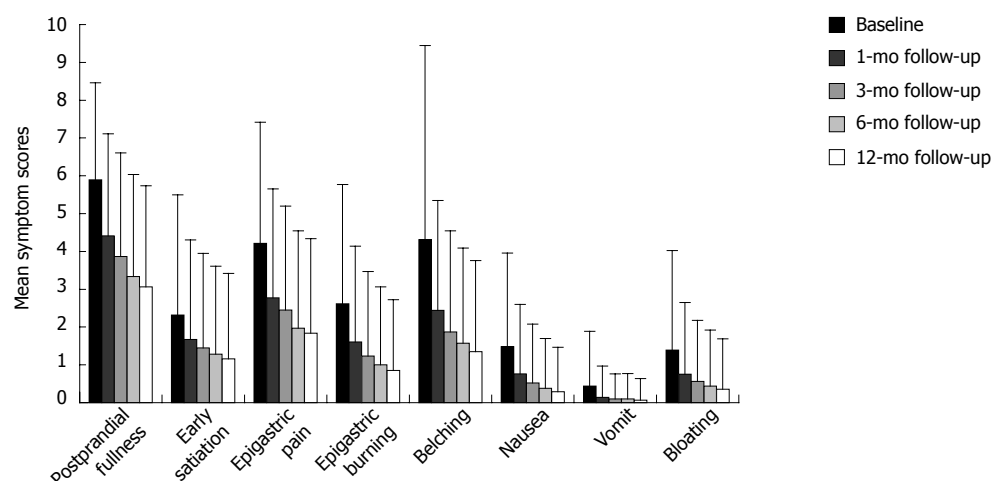


Figure 2 Comparison of dyspeptic symptoms between initial visit and at four follow-ups of repeated measures.

between 1 mo and 3 mo follow-up, $P = 0.330$; the difference between 3 mo and 6 mo follow-up, $P = 0.959$; the difference between 6 mo and 1 year follow-up, $P = 1.0$).

Factors associated with DSS at final follow-up (1-year follow-up)

Longitudinal associations: For patient characteristics at baseline, univariate correlates analysis revealed that history of abuse was associated with DSS at 1-year follow-up ($P = 0.025$), while no association was found for other variables such as sex, age, BMI, anxiety, depression, sleep disorder, *H. pylori* status, DSS at baseline, and drug treatment before baseline (Table 2). Multiple linear regression analysis showed no relationship between DSS at 1-year follow-up and patient characteristics at baseline (Table 2).

Horizontal associations: For patient characteristics at 1-year follow-up, univariate correlates analysis found that age ($P < 0.001$), alcohol consumption ($P = 0.024$), anxiety ($P < 0.001$), depression ($P < 0.001$), sleep disorder ($P < 0.001$), bowel symptoms ($P < 0.001$), weight loss ($P < 0.001$), consulting a physician ($P < 0.001$), prokinetic use ($P < 0.001$), gastric mucosa protectant use ($P < 0.001$), antacid use ($P < 0.001$), and traditional Chinese medicine use ($P < 0.001$) were significantly associated with DSS (Table 3).

Multiple linear regression analysis showed that sex ($P < 0.001$), anxiety ($P = 0.018$), sleep disorder ($P = 0.019$), weight loss ($P < 0.001$), consulting a physician ($P < 0.001$) and prokinetic use ($P = 0.035$) were significantly associated with DSS, while age, depression, alcohol consumption, bowel symptoms, and use of gastric mucosa protectants, antacids and traditional Chinese medicine were not associated with it (Table 3).

DISCUSSION

To the best of our knowledge, this is the first published prospective study with Chinese patients to explore the

clinical course of FD, and evaluate potential risk factors associated with FD, using the Rome III criteria, both longitudinally and horizontally. We selected a large group of FD patients from five cities in China. After their initial visit, patients were followed up at 1, 3 and 6 mo and 1 year.

The sample size was large and we had a good response rate to all parts of the study. We compared the baseline characteristics between the follow-up population and those who were lost to follow-up. We found that men, alcohol users, those with higher educational level and better economic situation, and those who had consulted a physician were significantly more likely to be successfully followed up. This is consistent with previous reports^[20,21]. There were some demographic differences between responders and non-responders, but the magnitude of these differences was small and the individuals included in our follow-up study were broadly representative of the original enrolled FD patients, suggesting that the results of our study are persuasive.

The novel finding of our study was that the total DSS in FD patients showed a significant gradually reduced trend during 1 year follow-up, and similar differences were found for all individual symptoms. It seems that patients feel much better at the final follow-up and complain of less discomfort. Several previous studies reported improved symptoms during a period of follow-up, which is in line with our findings^[5]. Kindt *et al.*^[22], in a 5-year follow-up study, found that about half of FD patients reported disappeared or improved symptoms. Pajala *et al.*^[23] observed a marked reduction in DSS in FD patients in Finland after 1 year follow-up. Heikkinen *et al.*^[24], in a long-term perspective study, also concluded that the stability of the symptom-based subgroups over time was poor. However, all of these studies only compared two time points, while our study compared five points.

Furthermore, we identified risk factors that influenced the clinical course of FD. Over the past decade, the correlation between psychological factors and func-

Table 2 Longitudinal associations between functional dyspepsia patients' baseline characteristics and dyspeptic symptom score at 1-year follow-up

Variable (at baseline)	Longitudinal associations							
	Univariate correlates			Multiple linear regression				
	r^1	F^2	P	B	β	t	P	R^2_{Model}
Sex ³		3.489	0.062	0.161	0.009	0.208	0.835	0.019
Age	0.002		0.959	-0.007	-0.009	-0.224	0.823	
BMI	0.007		0.835	-0.024	-0.009	-0.248	0.804	
Smoking		1.894	0.169	1.228	0.058	1.368	0.172	
Alcohol consumption		0.02	0.887	-0.665	-0.035	-0.876	0.381	
Major mental stimulation		1.288	0.257	-0.421	-0.013	-0.365	0.715	
History of abuse		5.022	0.025 ⁴	-3.774	-0.062	-1.762	0.078	
Anxiety		0.106	0.745	0.897	0.030	0.777	0.437	
Depression		0.937	0.333	-1.549	-0.044	-1.157	0.248	
Sleep disorder		1.831	0.176	-0.683	-0.040	-1.131	0.259	
Bowel symptom		0.17	0.680	0.442	0.020	0.580	0.562	
<i>H. pylori</i> status		0.461	0.631	-0.269	-0.027	-0.782	0.434	
DSS	-0.014		0.667	-0.015	-0.018	-0.502	0.616	
Treatments in the previous months before baseline								
Consulting a physician		0.753	0.386	0.468	0.027	0.804	0.421	
Prokinetic use		0.077	0.782	-0.598	-0.034	-0.933	0.351	
Gastric mucosa protectant use		1.407	0.236	0.611	0.034	0.971	0.332	
Antacid use		1.381	0.24	0.589	0.034	0.906	0.365	
Anti- <i>H. pylori</i> therapy		1.014	0.314	0.431	0.018	0.539	0.590	
Traditional Chinese medicine use		0.005	0.945	-0.025	-0.001	-0.042	0.966	

¹Pearson's correlation; ²Non-parametric one-way ANOVA; ³Male = 0, female = 1 reference category: female; ⁴Significant variables ($P < 0.05$). BMI: Body mass index; *H. pylori*: *Helicobacter pylori*; DSS: Dyspeptic symptom score.

Table 3 Horizontal associations between functional dyspepsia patients' baseline characteristics and dyspeptic symptom score at 1-year follow-up

Variable (at 1-yr follow-up)	Horizontal associations							
	Univariate correlates			Multiple linear regression				
	r^1	F^2	P	B	β	t	P	R^2_{Model}
Sex ³		3.489	0.062	0.585	0.033	6.356	< 0.001 ⁴	0.98
Age	0.139		< 0.001 ⁴	-0.002	-0.002	-0.456	0.649	
Time of follow-up (mo)	-0.035		0.288	-0.121	-0.008	-1.837	0.067	
Smoking		1.109	0.293	-0.242	-0.009	-1.533	0.126	
Alcohol consumption		5.132	0.024 ⁴	0.204	0.008	1.346	0.179	
Anxiety		13.257	< 0.001 ⁴	0.292	0.015	2.373	0.018 ⁴	
Depression		27.452	< 0.001 ⁴	-0.052	-0.002	-0.392	0.695	
Sleep disorder		69.219	< 0.001 ⁴	0.216	0.012	2.346	0.019 ⁴	
Bowel symptom		51.053	< 0.001 ⁴	0.185	0.007	1.377	0.169	
<i>H. pylori</i> status		1.563	0.210	-0.035	-0.003	-0.759	0.448	
Treatments during 1-yr follow-up period								
Consulting a physician		224.718	< 0.001 ⁴	0.893	0.051	9.168	< 0.001 ⁴	
Prokinetic use		59.340	< 0.001 ⁴	0.200	0.012	2.113	0.035 ⁴	
Gastric mucosa protectant use		22.857	< 0.001 ⁴	-0.014	-0.001	-0.147	0.883	
Antacid use		19.313	< 0.001 ⁴	-0.023	-0.001	-0.266	0.790	
Anti- <i>H. pylori</i> therapy		1.825	0.177	-0.075	-0.003	-0.635	0.526	
Traditional Chinese medicine use		50.799	< 0.001 ⁴	-0.062	-0.004	-0.755	0.450	
Weight loss during 1-yr follow-up period	0.988		< 0.001 ⁴	1.040	0.961	186.775	< 0.001 ⁴	

¹Pearson's correlation; ²Non-parametric one-way ANOVA; ³Male = 0, female = 1 reference category: female; ⁴Significant variables ($P < 0.05$). BMI: Body mass index; *H. pylori*: *Helicobacter pylori*; DSS: Dyspeptic symptom score.

tional gastrointestinal disorders has been confirmed in several clinical case-control studies^[25,26]. Koloski *et al*^[27] found that anxiety was an evident independent predictor for FD. Aro *et al*^[28], in a Swedish population-based study, showed that anxiety but not depression was linked to FD and PDS but not to EPS. In the present study, anxi-

ety at 1-year follow-up was also found to be horizontally associated with DSS, which is in keeping with previous studies.

Sleep disorder is a common phenomenon in all FD patients. Dyspeptic symptoms can interfere with sleep, and disrupted sleep may also potentially exacerbate FD

symptoms due to the hyperalgesic effect of sleep loss. Cremonini *et al.*^[14], in a study involving 3228 respondents, found that sleep disturbances were linked to both upper and lower gastrointestinal symptoms in the general population. Lacy *et al.*^[15] revealed that there was a relationship between FD and sleep disorder, and sleep disorder in FD patients appeared to be associated with symptom severity and higher levels of anxiety. We also discovered an association between sleep disorder at 1-year follow-up and FD outcome.

Recent cross-sectional population studies discovered that weight loss correlated most strongly with early satiety, followed by nausea and vomiting^[29]. A longitudinal study in Belgium found that weight loss was independently associated with FD-specific quality of life at follow-up, and there was a trend association between weight loss and DSS at follow-up^[22]. In this study, we did not have information about weight difference between dyspepsia symptom onset and initial visit. However, we collected data on patients' weight at baseline and at final follow-up, and observed that weight loss during 1 year follow-up was independently associated with DSS.

We showed an association between sex and FD outcome, indicating that women may have higher DSS at 1-year follow-up than men have, which is consistent with a cross-sectional study in Taiwan^[30]. There was no association between *H. pylori* status and DSS at 1-year follow-up, which is similar to another prospective 2-year follow-up study from Taiwan^[31].

An important finding in our study was that many individuals reported persistent symptoms despite consultation and prokinetic use during 1 year follow-up. Similarly, two recent studies have also reported persistence of symptoms in drug-treated patients^[32,33]. It is probable that patients consulting a physician have the most severe symptoms, and they often take prescribed drugs on an on-demand basis. In addition, most individuals ($n = 511$, 54% of follow-up patients) in our study had a prescription of prokinetic during 1 year follow-up. These may be the reasons why patients consulting a physician and taking prokinetic still have continuous symptoms or even more severe symptoms.

In bivariate analysis, we also found a correlation between history of abuse and DSS at 1-year follow-up, which was similar to several other characteristics (*i.e.*, age, alcohol consumption, depression, bowel symptoms, and use of gastric mucosa protectants, antacids and traditional Chinese medicine during 1 year follow-up period). However, this correlation was not found in multiple linear regression analysis, indicating that it was weak.

In conclusion, in this large sample of individuals with FD, 89.9% of patients completed all four follow-ups, and the average duration of follow-up was 12.24 ± 0.59 mo. During 1 year follow-up, the total DSS in FD patients showed a significant gradually reduced trend, and similar differences were found for all individual symptoms. Female sex, anxiety, sleep disorder, weight loss, consulting a physician, and prokinetic use during 1

year follow-up were associated with outcome. Our study described the fluctuations in symptoms and found that several associated factors affected outcome. We believe that these findings provide evidence for the role of psychosocial factors in determining long-term clinical course in patients with FD. In the future, more research is needed to confirm and extend our study.

COMMENTS

Background

Functional dyspepsia (FD) is a chronic functional gastrointestinal disorder, and it has a significant impact on quality of life and imposes a substantial economic burden on society. However, the clinical course and risk factors for FD remain poorly studied.

Research frontiers

In the present study, the authors selected a large group of FD patients from five cities in China and explored the clinical course and risk factors for FD both longitudinally and horizontally.

Innovations and breakthroughs

Some cross-sectional population studies have discovered several risk factors associated with FD. This is believed to be the first follow-up study showing that the total dyspeptic symptoms score and single symptom score in FD patients present a significant gradually reduced trend, and female sex, anxiety, sleep disorder, weight loss, consulting a physician, and prokinetic use during 1-year follow-up were associated with outcome.

Applications

The study described the fluctuations in dyspeptic symptoms and found several factors were associated with the outcome. This may provide evidence for the role of psychosocial factors in determining the long-term clinical course of patients with FD.

Terminology

FD is a highly prevalent gastrointestinal disorder that is defined by the presence of symptoms thought to originate in the gastroduodenal region, without identifiable cause by routine diagnostic methods.

Peer review

This is a follow-up study evaluating the clinical course and potential risk factors for FD. This is an interesting article discussing an important area in functional gastrointestinal disorders.

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