The psychological results of 438 patients with persisting GERD symptoms by Symptom Checklist 90-Revised (SCL-90-R) questionnaire

Ping Li, MD, PhD, Fei Wang, MM, Guo-zhong Ji, MD, PhD, Lin Miao, MD, MM, Sihong You, MD, PhD, Xia Chen, MD, PhD

Abstract

Persisting gastroesophageal reflux disease (GERD) symptoms affect mental state and social activities and mental disorders likewise play a crucial role on GERD symptoms. The aim of this study was to analyze the data of Symptom Checklist by 90-Revised (SCL-90-R) questionnaire in patients with persisting GERD symptom and to explore the impact of psychological factors on them.

The patients accepted SCL-90-R questionnaire survey, following endoscopy, high-resolution manometry (HRM) and ambulatory impedance-pH monitoring. Based on these results, we divided patients into different groups. The result of SCL-90-R was also compared by degree of acid reflux, symptoms, symptom duration, and gender.

The data from 438 patients were analyzed. All patients were divided into reflux esophagitis (RE) (63, 14.38%); nonerosive gastroesophageal disease (NERD) (106, 24.20%); functional heartburn (FH) (123, 28.08%), and hypersensitive esophagus (HE) (67, 15.29%); depression (DES) (5, 1.14%); hypertensive (10, 3.42%); weak peristalsis (14, 3.20%); achalasia (50, 11.42%). There were significant differences between varied groups judging by DEP, anxiety (ANX), paranoia ideation (PAR), psychoticism (PSY), and global severity index (GSI) domains (all \( P < .05 \)). The patients with \( ≥ 2 \) years symptom duration presented more scores in DEP, ANX, and PSY (all \( P < .05 \)). Compared to typical symptoms (\( n = 185 \)), GERD typical plus atypical symptoms (\( n = 253 \)) had higher scores of somatization (SOM), ANX, PSY and GSI (all \( P < .05 \)). Women were found to have significantly higher scores than men in all domains (all \( P < .05 \)).

Our results find significant differences between varied patients with different diagnosis in DEP, ANX, PAR, PSY domains, and GSI. Long symptom duration, typical plus atypical symptoms, and female are more risky for psychological disorders.

Abbreviations: ANX = anxiety, DEP = depression, DES = diffuse esophageal spasm, FH = functional heartburn, GERD = gastroesophageal reflux disease, GSI = global severity index, HE = hypersensitive esophagus, HOS = hostility, HRM = high-resolution manometry, I-S = interpersonal sensitivity, NERD = nonerosive gastroesophageal disease, O-C = obsessive-compulsive behavior, PAR = paranoia ideation, PHOB = phobic anxiety, PPI = proton pump inhibitor, PSY = psychoticism, RE = reflux esophagitis, SCL-90-R = Symptom Checklist-90-R, SOM = somatization.

Keywords: gastroesophageal reflux disease (GERD), high-resolution manometry (HRM), impedance-pH monitoring, refractory proton pump inhibitor (PPI) symptoms, Symptom Checklist 90-Revised (SCL-90-R) questionnaire

1. Introduction

Due to changes in environmental conditions, recent epidemiological evidences suggest that the incidence of gastroesophageal reflux disease (GERD) is increasing in both Asian and Western countries.\(^{[1,2]}\) Therapeutic strategy for GERD mainly involves the use of proton pump inhibitors (PPIs) to control symptoms. Troublesome GERD symptoms persist in 20% to 30% of patients despite daily treatment with a standard proton pump inhibitor (PPI) dose.\(^{[3]}\) Persisting GERD symptoms cause discomfort, impair quality of life, and affect mental state and social activities. Likewise, the subsequent development of mental disorders, such as: anxiety, depressive, also play a crucial role on GERD symptoms deterioration and have a negative effect on people’s quality of life.\(^{[4]}\)

The Symptom Checklist 90-Revised (SCL-90-R) is an international, widely used, self-report questionnaire of multidimensional complaints with normative data for healthy control subjects and psychiatric patients. Some medical groups applied SCL-90-R to evaluate the psychological state of patients with chronic disease.\(^{[5,6]}\) Previous studies suggest that the SCL-90-R questionnaire could be useful in investigating psychological factors and have made recommendations for psychosocial...
approaches in clinical practice. However, data from patients with persisting refractory GERD symptom based on SCL-90-R questionnaire scarcely have been shown.

This study focused on the psychological state of refractory GERD patients evaluated by SCL-90-R. We intended to find the differences between several varied conditions of refractory GERD symptom; therefore, to discover whether SCL-90-R would be useful in differentiate diagnosis for refractory GERD and whether SCL-90-R would be a new, simple method for pointing out potential reason by screening patients with GERD in a community hospital. Consequently, it may be helpful for gastroenterologist to choose relatively precise diagnostic approaches.

2. Methods

The target patients were all with persisting GERD symptoms after an 8-week trial of once-daily PPIs therapy from October 2010 to November 2015.

Exclusion criteria were as follows: previous esophageal, gastric, or duodenal surgery; gastrointestinal organic disease or significant comorbidity such as severe hepatic or renal disease, or gastrointestinal bleeding; oncologic diseases; previous diagnosis of psychopathological; current psychopharmacological treatment; gastrointestinal functional disorders.

The methodological approach was based on administration of the following test: the Symptom Check List SCL-90-R,[10] upper gastrointestinal endoscopy, high-resolution manometry (HRM, Given Imaging, Los Angeles, CA), 24-hour impedance-pH monitoring (Given Imaging, Los Angeles, CA). Data of HRM and impedance-pH monitoring analysis were performed using Medical Measure Systems pH Analysis software (Mano View software; Sierra Scientific Instrument Inc, Los Angeles, CA).

The Symptom Check List SCL-90-R comprises 90 items that assess psychopathological or somatic disturbances on a 4-point scale ranging from 0 (absence of the symptom) to 4 (maximum disturbance). The 90 items are grouped into 9 scales labeled as obsessive-compulsive behavior (O-C); interpersonal sensitivity (I-S); depression (DEP); anxiety (ANX); hostility (HOS); phobic anxiety (PHOB); paranoid ideation (PAR); and psychoticism (PSY). Each of the 9 symptom dimensions is reassessed with 6 to 13 items. The score on each dimension represents the mean score of all items of the dimension and directly reflects the severity of the mental health problem. Subscale scores ≥ 2 were suggestive of potential mental health issues. The global severity index (GSI) is a mean score of all 90 items.[11]

Patients groups: based on the results of endoscopy, HRM and impedance-pH monitoring, patients were divided into subgroups as follows: reflux esophagitis (RE); nonerosive gastroesophageal reflux disease (NERD); hypersensitive esophagus (HE); functional heartburn (FH); diffuse esophageal spasm (DES); hypertensive; weak peristalsis; and achalasia. The diagnosis made and classified accordingly to the Chicago classification and previously published criteria.[12,13]

The protocol for the research project was approved by the Second Affiliated Hospital of Nanjing Medical University Institutional Ethics Committee within which the work was undertaken and that it conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000).

2.1. Statistical analysis

Data manual analysis was performed independently by 2 investigators unaware of the status of individuals. The data

were presented as mean±SD unless otherwise specified. Statistical analysis included Pearson’s chi-square test for categorical variables and ANOVA for continuous variables. All statistical calculations were performed using SPSS 13.0. A P<.05 was considered significant and all reported P values are 2 sided.

3. Results

3.1. Demographic and clinical characteristics

A total of 438 patients (137 males, 301 females, age 51.42±17.30 years) were analyzed in this study (Table 1). Symptom duration of these patients was 4.02±1.45 years. There were 271 (61.87%) patients with heartburn and 239 (54.57%) with regurgitation, 189 (43.15%) with retrosternal discomfort and pain (Table 1). All patients were divided into: RE (63, 14.38%); NERD (106, 24.20%); FH (123, 28.08%); and HE (67, 15.29%); DES (5, 1.14%); hypertensive (10, 3.42%); weak peristalsis (14, 3.20%); achalasia (10, 2.26%).

Table 1 Demographics and clinical characteristics.

| Characteristics | n  | %  |
|-----------------|----|----|
| Age, years      |    |    |
| range           | 19–83 |   |
| Gender          |    |    |
| Male            | 137| 31.28 |
| Female          | 301| 68.72 |
| BMI             | 23.42±10.37 |
| RE              | 63 | 14.38 |
| NERD            | 106 | 24.20 |
| HE              | 123 | 28.08 |
| FH              | 67 | 15.29 |
| DES             | 5  | 1.14  |
| Hypertensive    | 10 | 3.42  |
| Weak peristalsis| 14 | 3.20  |
| Achalasia       | 49 | 11.19 |
| Smoking         | 142 | 32.42 |
| Alcohol consumption drug history | 145 | 33.10 |
| Calcium ion antagonist | 179 | 40.87 |
| Aspirin         | 153 | 34.93 |
| Hypnotics drug  | 51 | 11.64 |
| past medical history | 253 |   |

were presented as mean±SD unless otherwise specified. Statistical analysis included Pearson’s chi-square test for categorical variables and ANOVA for continuous variables. All statistical calculations were performed using SPSS 13.0. A P<.05 was considered significant and all reported P values are 2 sided.

3.2. SCL-90-R questionnaire survey

We investigated the scores of 9 domains of SCL-90-R in varied groups (Table 2). The data showed that there were significant
Scores in different groups.

| Domain | RE (n=63) Mean ± SD | HE (n=67) Mean ± SD | FH (n=123) Mean ± SD | NERD (n=106) Mean ± SD | Achalasia (n=50) Mean ± SD | Hypertensive (n=10) Mean ± SD | DES (n=5) Mean ± SD | Weak (n=14) Mean ± SD |
|--------|-----------------|-----------------|-----------------|-----------------|----------------|----------------|----------------|----------------|
| SOM    | 1.30 ± 0.58     | 1.46 ± 0.62     | 1.57 ± 0.67     | 1.40 ± 0.62     | 1.54 ± 0.66     | 1.66 ± 0.72     | 1.20 ± 0.59     | 1.46 ± 0.90     |
| O-C    | 1.50 ± 0.54     | 1.42 ± 0.64     | 1.55 ± 0.63     | 1.50 ± 0.63     | 1.62 ± 0.73     | 1.39 ± 0.56     | 1.94 ± 0.70     | 1.62 ± 0.73     |
| I-S    | 1.43 ± 0.67     | 1.35 ± 0.66     | 1.38 ± 0.57     | 1.40 ± 0.59     | 1.48 ± 0.71     | 1.57 ± 0.75     | 1.20 ± 0.59     | 1.60 ± 0.69     |
| DEP    | 1.48 ± 0.64     | 1.51 ± 0.65     | 1.77 ± 0.59     | 1.80 ± 0.59     | 1.76 ± 0.66     | 1.27 ± 0.54     | 1.65 ± 0.67     | 1.61 ± 0.81     |
| ANX    | 1.50 ± 0.60     | 1.46 ± 0.70     | 1.69 ± 0.62     | 1.70 ± 0.53     | 1.87 ± 0.66     | 1.34 ± 0.57     | 1.57 ± 1.06     | 1.72 ± 0.73     |
| HOS    | 1.44 ± 0.56     | 1.40 ± 0.62     | 1.40 ± 0.61     | 1.39 ± 0.67     | 1.35 ± 0.56     | 1.40 ± 0.84     | 1.20 ± 0.59     | 1.51 ± 0.75     |
| PHOB   | 1.48 ± 0.64     | 1.47 ± 0.62     | 1.42 ± 0.58     | 1.47 ± 0.64     | 1.36 ± 0.68     | 1.20 ± 0.57     | 1.57 ± 1.06     | 1.37 ± 0.56     |
| PAR    | 1.27 ± 0.49     | 1.15 ± 0.47     | 1.27 ± 0.47     | 1.32 ± 0.57     | 1.12 ± 0.44     | 0.96 ± 0.36     | 0.56 ± 0.51     | 1.36 ± 0.51     |
| PSY    | 1.64 ± 0.47     | 1.31 ± 0.53     | 1.23 ± 0.51     | 1.27 ± 0.50     | 1.59 ± 0.57     | 1.58 ± 0.60     | 1.67 ± 0.48     | 1.51 ± 0.50     |
| GSI    | 1.04 ± 0.41     | 1.01 ± 0.42     | 1.02 ± 0.38     | 1.18 ± 0.38     | 1.07 ± 0.44     | 1.17 ± 0.47     | 0.94 ± 0.43     | 1.11 ± 0.44     |

ANX = anxiety, O = confidence interval, DEP = depression, GSI = global severity index, HOS = hostility, I-S = interpersonal sensitivity, O-C = obsessive–compulsive behavior, PAR = paranoid ideation, PHOB = phobic anxiety, PSY = psychoticism, SOM = somatization.

* means P < 0.05 between groups.

doctoral differences between varied groups judging by DEP, ANX, PAR, PSY, and GSI domains (all P < 0.05).

In DEP domain, the score in RE group was less than in NERD, FH, achalasia groups (all P < 0.05); the score in NERD was more than in HE and hypertensive groups (all P < 0.05); the score in FH was more than in HE and hypertensive groups (all P < 0.05); the score in achalasia was more than in HE as well as hypertensive groups (all P < 0.05).

About ANX domain, we found RE group had less score than in NERD and achalasia groups (all P < 0.05); NERD group had more than HE group (P < 0.05); FH group had more score than HE group (P < 0.05); achalasia had more score than HE and hypertensive groups (all P < 0.05).

For PSY, the score of achalasia group showed higher level than RE, NERD, FH, and HE groups (all P < 0.05); the score of FH group was more than hypertensive group (P < 0.05).

In PAR, NERD group had more score than HE, hypertensive and achalasia groups (all P < 0.05), and hypertensive group had more score than DES group (P < 0.05).

According to the result of GSI domain, the data revealed that the level of NERD was higher than RE, FH, and HE groups (all P < 0.05).

Apart that, we compared the 9 domains with DeMeester value ≥14.72, n=114 and normal (<14.72, n=245) values with no statistical significance (P > 0.05) (Fig. 1). However, we found statistical significance between the patients with less GERD symptoms duration (<2 years, n=95) and with more duration (≥2 years, n=343). The patients with more duration presented more scores in DEP, ANX, and PSY (all P < 0.05) (Fig. 2). But the score of PAR was lower in ≥2 years group (P < 0.05). The scores for the 9 domains of the SCL-90-R are given with GERD symptoms in Fig. 3. Subjects with GERD typical plus atypical symptoms (n=253) had higher scores compared to subjects only with typical symptoms (n=185) in the next domains: SOM, ANX, PSY, and GSI (all P < 0.05). Evaluating each domain separately based on gender, women were found to have significantly higher scores than men in all domains (all P < 0.05) (Fig. 4).

Figure 1. SCL-90-R scores based on DeMeester value. No differences were detected in 9 domains and GSI between DeMeester value ≥14.72 and DeMeester value < 14.72. GSI = global severity index, SCL-90-R = Symptom Checklist-90-R.

Figure 2. SCL-90-R scores depending on symptom duration. * means P < 0.05. Significant differences were seen in DEP, ANX, PAR and PSY domains. ANX = anxiety, DEP = depression, PAR = paranoid ideation, PSY = psychoticism, SCL-90-R = Symptom Checklist-90-R.

Figure 3. SCL-90-R scores based on symptom. * means P < 0.05. Significant differences were seen in SOM, ANX and PSY domains and GSI. ANX = anxiety, PSY = psychoticism, SCL-90-R = Symptom Checklist-90-R, SOM = somatization.
4. Discussion

Psychosocial factors can affect the development of diseases, symptoms, responses to treatment, and quality of life. Researchers evaluated the psychological status of patients with chronic disease using SCL-90-R questionnaire. A link of GERD and psychopathological features has already been demonstrated by several studies. We analyzed the data from the patients with refractory GERD symptoms in order to acquire their psychological characteristics, which may be helpful for making diagnosis and clinical strategy.

On purpose of determining which psychosocial factor probably involved into refractory GERD symptoms, we studied the 9 domains of the SCL-90-R questionnaire in patients with different diagnoses who presented refractory GERD symptoms. In this study, O-S and I-S, which are stable personality characters and are referred as personality, were not found statistical significance between these patients. But in DEP, ANX, PAR, PSY, and GSI domains, the data had differences. We discovered the scores of these domains in NERD, FH, and HE groups were higher than those of asymptomatic patients on all items of SCL-90-R,[22] we chose patients only with typical GERD symptom to compare with those with typical plus atypical GERD symptom. Our aim was to acquire more precise information about the relationship between mental disorder and GERD symptom. From the data, which complimented previous studies to a certain extent, we assume that companion with other atypical GERD symptoms means more risky for psychological diseases.

The analysis of symptoms duration in this study showed that the patients with more duration had more problems of DEP, ANX, and PSY. Most patients suffered from refractory GERD symptom have long duration and evaluating the psychological status of these patients should be taken more concerns in further studies. Considering of gender difference, we investigated the data divided by female and male. Our results are consistent with Núñez-Rodríguez MH’s study[17] women were found to have significantly higher scores than men in all domains by SCL-90-R. Due to more researches pay attention to gender difference in chronic diseases development[23–25] in recent decades, the difference between female and male may need more investigations.

Some restrictions must be acknowledged regarding the measurement of mental disorders with the SCL-90-R in the present study. The interviewing, diagnosing, and rating were done by experts in our gastroenterology department. Although our research team acquired assistance of psychologists, the results were likely to have a little bias. Moreover, the samples in this study were regional instead of a nationally representative. Differences across cities and countries may occur due to differences in sociodemographics. The large scale linked to multi-canter study needs to be carried out in further studies. Despite these limitations, the goals for testing the psychological status of the patients with refractory GERD symptoms by the SCL-90-R were achieved. The questionnaire showed acceptable qualities for evaluating mental health disorders in the first step. The use of SCL-90-R supplemented by following endoscopy, HRM, and pH monitoring may enhance the precision of differential diagnosis for refractory GERD symptoms.

In conclusion, we firstly observed the psychological disorders of the patient with different diagnosis presented refractory GERD symptom. We think that psychological factors have an unignorable significance in the research field. For these patients, the treatment for psychological disorder may help them alleviating symptom and improving the quality of life. The further question is whether all patients with psychological problem should accept suitable treatment and how to define the indication. Undoubtedly, there is a need for further research.

References
[1] Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol 2013;108:308–28.
[2] Fock KM, Talley N, Goh KL, et al. Asia-Pacific consensus on the management of gastro-oesophageal reflux disease: an update focussing on reflux disease and Barrett’s oesophagus. Gut 2016;65:1402–15.
[3] Fass R. Proton-pump inhibitor therapy in patients with gastro-oesophageal reflux disease: putative mechanisms of alure. Drugs 2007;67:1521–30.
[4] You ZH, Perng CL, Hu LY, et al. Risk of psychiatric disorders following gastroesophageal reflux disease: a nationwide population-based cohort study. Eur J Intern Med 2015;26:534–9.
[5] Cardin F, Ambrosio, Arnodio P, et al. Quality of life and depression in a cohort of female patients with chronic disease. BMC Surg 2012;12(suppl 1):S10.
[6] Bakir S1, Kinis V, Bez Y, et al. Mental health and quality of life in patients with chronic otitis media. Eur Arch Otorhinolaryngol 2013;270:521–6.
[7] Eitner S, Wichmann M, Schlegel A, et al. Clinical study on the correlation between psychogenic dental prosthesis incompatibility, oral stereognosis, and the psychological diagnostic tools SCL-90-R and CES-D. Int J Prosthodont 2007;20:538–45.

[8] Levy RL, Olden K, Naliboff B, et al. Psychosocial aspects of the functional gastrointestinal disorders. Gastroenterology 2006;130:1447–58.

[9] Paice JA, Ferrell B. The management of cancer pain. CA Cancer J Clin 2011;61:157–82.

[10] Lipman LR, Covi RSL. SCL-90: an outpatient psychiatric rating scale–preliminary report. Psychopharmacol Bull 1973;9:13–28.

[11] Derogatis LR, Rickels K, Rock A. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976;128:280–90.

[12] Bredenoord AJ, Fox M, Kahrilas PJ, et al. International High Resolution Manometry Working Group. Chicago classification criteria esophageal motility disorders defined in high resolution esophageal pressure topography. Neurogastroenterol Motil 2012;24:57–65.

[13] Mittal RK, Karstens A, Leslie E, et al. Ambulatory high-resolution manometry, lower esophageal sphincter lift and transient lower esophageal sphincter relaxation. Neurogastroenterol Motil 2012;24:40–6.

[14] Lim CH, Choi MG, Baeg MK, et al. Symptom characteristics and psychosomatic profiles in different spectrum of gastroesophageal reflux disease. Gut Liver 2014;8:165–9.

[15] Jansson C, Nordenstedt H, Wallanger M-A, et al. Severe gastroesophageal reflux symptoms in relation to anxiety, depression and coping in a population-based study. Aliment Pharmacol Ther 2007;26:681–91.

[16] Lee YC, Wang HP, Chiu HM, et al. Comparative analysis between psychological and endoscopic profiles in patients with gastroesophageal reflux disease: a prospective study based on screening endoscopy. J Gastroenterol Hepatol 2006;21:798–804.

[17] Núñez-Rodriguez MH, Miranda Svelo A. Psychological factors in gastroesophageal reflux disease measured by SCL-90-R questionnaire. Dig Dis Sci 2008;53:3071–5.

[18] Cardin F, Ambrosio F, Amadio P, et al. Quality of life and depression in a cohort of female patients with chronic disease. BMC Surg 2012;12 (suppl 1):S10.

[19] Nozu T, Komiyama H. Clinical characteristics of asymptomatic esophagitis. J Gastroenterol 2008;43:27–31.

[20] Neumann H, Monkmuller K, Kandulski A, et al. Dyspepsia and IBS symptoms in patients with NERD, ERD and Barrett’s esophagus. Dig Dis Sci 2008;56:243–7.

[21] Rey E, Elosa-Olazo CM, Rodríguez-Artalejo F, et al. Prevalence of atypical symptoms and their association with typical symptoms of gastroesophageal reflux in Spain. Eur J Gastroenterol Hepatol 2006;18:969–75.

[22] Lee SP, Lee KN, Lee OY, et al. The relationship between existence of typical symptoms and psychological factors in patients with erosive esophagitis. J Neurogastroenterol Motil 2012;18:284–90.

[23] Robles PG, Brooks D, Goldstein R, et al. Gender-associated differences in pulmonary rehabilitation outcomes in people with chronic obstructive pulmonary disease: a systematic review. J Cardiopulm Rehabil Prev 2014;34:87–97.

[24] Baggio G, Corsini A, Florenzi A, et al. Gender medicine: a task for the third millennium. Clin Chem Lab Med 2013;51:713–27.

[25] Kotkova P, Weir P. Psychiatric factors related to sexual functioning in patients with Parkinson’s disease. Clin Neurol Neurosurg 2013;115:419–24.