Composite score of reflux symptoms in diagnosis of gastroesophageal reflux disease

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Abstract

AIM: To evaluate the significance of the composite score of reflux symptoms in the diagnosis of gastroesophageal reflux disease (GERD), and to determine the relationship of the composite score with reflux esophagitis (RE) and pathological gastroesophageal reflux (PGER).

METHODS: Upper digestive endoscopy and/or 24-h esophageal pH monitoring were performed in 244 subjects. Of these, 54 were consecutive patients attending our clinic with symptoms suggestive of GERD, and 190 were randomly selected from 2532 respondents who participated in our previous general population-based study on GERD. A standardized questionnaire was used to classify both the frequency and severity of typical symptoms of GERD (heartburn, acid and food regurgitation) using a 4-score scale, and the composite score of main reflux symptoms (score index: SI, range from 0 to 18) were calculated for every subject. RE was diagnosed according to the Savary-Miller criteria. Subjects with abnormal pH-metry (DeMeester scale, and the composite score of main reflux symptoms (score index: SI, range from 0 to 18) were calculated for every subject. RE was diagnosed according to the Savary-Miller criteria. Subjects with abnormal pH-metry (DeMeester score more than 14.7) were considered to have PGER. GERD patients were defined as the subjects with RE and/or PGER.

RESULTS: The sensitivity of SI in the diagnosis of GERD was inversely associated with SI, but the specificity tended to increase with increased SI. With the cut-off of 8, the SI achieved the highest accuracy of 70.0%, with a sensitivity of 78.6% and a specificity of 69.2% in diagnosing GERD, followed by the cut-off of 3, which had an accuracy of 62.1%, a sensitivity of 96.4% and a specificity of 34.6%. The prevalence of RE, PGER and GERD was strongly associated with increased SI (P<0.01), but there was no significant association between the severity of RE and SI (P>0.05). Among patients with RE, 69.2% had PGER, and 30.8% were confirmed to have negative findings of pH monitoring. Among patients with PGER, 52.9% were identified to have RE and 47.1% had negative endoscopic findings in esophagus.

CONCLUSION: According to the composite score of main reflux symptoms, the diagnosis of GERD can be made without further tests in most cases. However, 24-h esophageal pH monitoring and upper digestive endoscopy are still indicated in patients with mild and atypical symptoms.

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a very common disorder both in China[12-1] and Western countries[3-8]. The disease results from the abnormal reflux of gastric contents into the distal esophagus causing symptoms in most patients and subsequent mucosal damage in some patients. It has been proved that chronic GERD tends to develop to Barrett’s esophagus associated with an increased risk of esophageal adenocarcinoma[9-13]. Heartburn and regurgitation are the typical symptoms of GERD, and 24-h esophagus pH monitoring and upper digestive endoscopy are the main methods to confirm the diagnosis. These examinations, however, are inconvenient and not universal in many hospitals of China, especially 24-h esophagus pH monitoring. Although the relationship between reflux symptoms and GRED were evaluated by some clinical studies, the results varied considerably because the symptoms were quantified by different criteria and methods[14-16]. As far as we know, data about the relationship between the combination of main reflux symptoms and proven GERD are lacking. The aim of this study was to establish a standard system to quantify the severity and frequency of typical reflux symptoms, and to evaluate the role of the composite score of main reflux symptoms in the diagnosis of GERD, and to determine the association between the composite score and reflux esophagitis (RE), pathological gastroesophageal reflux (PGER), and GERD.

MATERIALS AND METHODS

Subjects

Two hundred and forty-four subjects were included in this study. Among these, 54 were consecutive patients (32 men and 22 women; mean age, 45.3±13.2 years) who attended our clinic with symptoms suggestive of GERD and underwent both 24-h esophageal pH monitoring and upper digestive endoscopy. The remaining 190 subjects were randomly selected from 2532 respondents who were previously enrolled in our general population-based study on GERD, according to the composite score (score index, SI) of main reflux symptoms (Table 1), and who underwent 24-h esophageal pH monitoring (50 subjects) or/and upper digestive endoscopy (140 subjects). Patients with previous foregut surgery and other systemic disorders affecting the gastrointestinal motility were excluded. Five selected respondents (3 in the normal group and 1 in the mild symptom group) refused to participate in this study, 1 (normal group) had intolerance to pH monitoring, and 1(normal group) did not complete the evaluation. All of the 7 incomplete respondents were replaced by our clinic patients with same gender, SI, and similar age (±5 years). There were no appreciable differences in age or gender among these groups (P>0.05).

Questionnaire

A standardized questionnaire based on our previous work was...
Table 1 Gender and age distribution of 190 subjects in symptom severity groups

| Severity of symptoms | Responders | Upper digestive endoscopy | 24-h pH monitoring |
|----------------------|------------|---------------------------|-------------------|
|                      | Subjects   | Mean age (yr)             | Subjects          |
|                      | Men/Women  |                          | Men/Women         |
| Normal               | 2 102      | 45.5±9.9                  | 15                |
| Mild                 | 332        | 46.1±14.4                 | 15                |
| Moderate             | 74         | 47.4±9.6                  | 10                |
| Severe               | 24         | 49.1±10.2                 | 10                |
| Total                | 2 532      | 47.0±11.0                 | 50                |

Table 2 Relationship between SI and RE, PGER, GERD

| Criteria of SI | Endoscopic examination (RE%) | pH monitoring (PGER%) | Endoscopic or/and pH examination (GERD%) |
|---------------|------------------------------|-----------------------|----------------------------------------|
| Normal (SI = 0-2) | 40 (0.0)                     | 15 (0.0)              | 55 (0.0)                               |
| Mild (SI = 3-7) | 40 (3.7)                     | 12 (13.3)             | 52 (7.69)                              |
| Moderate (SI = 8-12) | 40 (27.5)                        | 4 (40.0)               | 45 (26.7)                              |
| Severe (SI ≥13) | 20 (66.5)                     | 6 (60.0)               | 24 (54.2)                              |

*P<0.05 and b*P<0.01 vs normal group.

Endoscopy

General upper digestive endoscopy was performed using a Pentax videodensoscope, and the same two gastrointestinal physicians made the diagnosis according to VHS videocassettes recorded.

Twenty-four hour esophageal pH monitoring

Twenty-four hour ambulatory esophageal pH monitoring was performed using a Synectic device. The pH electrode should be positioned 5 cm above the lower esophageal sphincter. Subjects were instructed to fill in diary cards regarding the time of meals, supine position and the time of symptoms experienced during the 24-h period. In addition, they were asked to press a button on the digital data logger at the beginning of each symptom episode. No restrictions were imposed on food and beverage intake or smoking.

Definitions

The following definitions for symptom categories and diseases were used. Only symptoms occurring in the past year before the interview were considered. Heartburn was defined as a burning pain or burning sensation behind the breastbone in the chest, acid regurgitation as a bitter or sour-tasting fluid coming into throat or mouth, food regurgitation as eaten foods coming into mouth. Heartburn, acid regurgitation and food regurgitation were considered to be the typical symptoms of GERD. Each of these symptoms was estimated according to its severity and frequency measured on a 4-score scale. Severity was assessed as follows: 0, none; 1, mild (could be ignored); 2, moderate (could not be ignored but did not affect lifestyle); 3, severe (affected lifestyle). The score of symptom frequency was estimated as follows: 0, none or less than one occasion per month on average; 1, several occasions once to three times a month; 2, several occasions (once to six times) a week; 3, one or more daily occasions. Based on the scores of severity and frequency of the main GERD symptoms, the composite score (SI: ranged from 0 to 18) of every subject was calculated.

RESULTS

Relationship between SI and its diagnostic accuracy for GERD

Among the 54 outpatients with symptoms suggestive of GERD, 28 patients (51.9%) were identified as GERD (16 patients with RE, 12 patients with PGER, 10 patients with RE and PGER), and 26 patients (48.1%) were normal, based on the findings of upper digestive endoscopy and 24-h esophageal pH monitoring. Figure 1 summarizes the relationship between criteria and its diagnostic accuracy for GERD compared with the diagnosis of endoscopy and pH monitoring. The sensitivity was inversely associated with increased SI, but the specificity tended to be higher with increased SI. The SI ≥8 had the highest accuracy (70.0%) for diagnosing GERD with a sensitivity of 78.6% and a specificity of 69.2%, followed by SI ≥13 with a specificity of 72.1%, a sensitivity of 96.4% and a specificity of 86.4%.

Relationship between SI and RE, PGER, GERD

As shown in Table 2, the rate of RE was the highest in the severe group, followed by moderate, mild and normal groups, and the results were similar to both PGER and GERD. The rate of RE, PGER and GERD was strongly associated with increased SI. In the severe and moderate groups, the frequency of RE, PGER and GERD was significantly higher than that of the normal group (P<0.05 or P<0.01).
have negative pH monitoring. Upper gastrointestinal tract endoscopy was performed in 34 patients with PGER, of them, 18 (52.9%) were identified to have RE, but the remaining 16 (47.1%) patients were proven to have a negative endoscopic finding in the esophagus. The results are summarized in Figure 3.

**DISCUSSION**

Gastroesophageal reflux disease is a common disease with many typical and atypical symptoms. A low pressure exerted by the lower esophageal sphincter (LES) and an increased frequency of transient LES relaxation might contribute to the development of GERD\(^\text{[17,19]}\). Esophageal testing, particularly 24-h pH monitoring has become the key to make the diagnosis and to ensure adequate acid suppression or prior to surgical therapy\(^\text{[20]}\). Although the test could yield accurate and reliable information, it is inconvenient for patients. The problem is whether all patients require 24-h esophageal pH monitoring to establish the diagnosis of GERD. If so, its use, however, is not popular and many hospitals in China are unable to perform this special testing. For these reasons, we are trying to develop a standard system to quantify the symptoms and to evaluate the accuracy of the combination of typical reflux symptoms in the diagnosis of GERD with the hope of eliminating the need for the monitoring.

Laboratory studies have demonstrated that there is a close relationship between classic reflux symptoms and esophageal acid exposure, but some clinical studies revealed that these symptoms were neither specific nor sensitive to the diagnosis of GERD\(^\text{[15,21-23]}\). For example, Tefera and his colleagues\(^\text{[21]}\) reported that moderate or severe heartburn could be used to diagnose GERD with a sensitivity of 68.42% and a specificity of 62.96%, and moderate or severe regurgitation with a sensitivity of 56.76% and a specificity of 65.08%. There were some common grounds in these clinical studies. These symptoms were evaluated separately. The frequency of each symptom was quantified but the severity was not considered. In our study, every typical symptom was estimated by quantifying both the frequency and the severity, and a combination score (SI) of all symptoms was calculated for every subject to exclude those subjects with trivial symptoms and to improve the accuracy of SI in the diagnosis of GERD.

We found that the sensitivity of the composite score of main reflux symptoms in the diagnosis of GERD was inversely associated with increased SI, but the specificity tended to be higher with increased SI. SI \(\geq 8\) had the highest accuracy of 70.0% for diagnosing GERD with a sensitivity of 78.6% and a specificity of 62.96%, and moderate or severe regurgitation with a sensitivity of 56.76% and a specificity of 65.08%. There were some common grounds in these clinical studies. These symptoms were evaluated separately. The frequency of each symptom was quantified but the severity was not considered. In our study, every typical symptom was estimated by quantifying both the frequency and the severity, and a combination score (SI) of all symptoms was calculated for every subject to exclude those subjects with trivial symptoms and to improve the accuracy of SI in the diagnosis of GERD.

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**Relationship between RE and PGER**

Of the 43 patients with RE, 26 patients underwent 24-h esophageal pH monitoring. Eighteen patients with RE (69.2%) complicated by PGER and 8 patients (30.8%) were confirmed to

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gastroenterological doctors to estimate the patients with typical reflux symptoms, especially in hospitals or clinics without objective tests. We suggest that patients with SI ≥ 8 may be treated pharmacologically combined with life style counseling. If the symptoms have not improved after 6 to 12 wk, 24-h pH monitoring and/or endoscopic examination should be performed, and if necessary, barium radiographing and manometry should be done.

Our study showed that the prevalence of RE, PGER and GERD was strongly associated with increased SI, but no significant association was found between the severity of RE and SI, indicating that patients with more severe reflux symptoms tend to have GERD, but the grade of esophagitis could not be evaluated on the basis of the severity of typical symptoms.

The present study also revealed that almost one third of patients with RE (30.8%) were confirmed to have negative pH monitoring and half of patients with PGER (47.1%) had negative endoscopic findings in the esophagus, the results were similar to previous studies. Excessive bile exposure of esophageal mucosa was the main cause of RE with normal acid exposure. We suggest that endoscopy-negative reflux disease (ENRD) should be treated as endoscopy positive GERD because longterm acid exposure would rapidly damage esophageal mucosa.

Patients with atypical symptoms such as cough, asthma, hoarseness, chest pain, and ear, nose and throat symptoms were not included in this study because they always had their first visit at specialized services. According to some studies the prevalence of GERD in patients with atypical symptoms ranged from 25% to 80%. We suggest that diagnostic tests such as upper digestive endoscopy and 24-h pH monitoring are a necessity for patients with atypical symptoms.

In conclusion, developing a criterion based on the composite score of typical reflux symptoms is useful to the diagnosis of GERD. Symptom questionnaire and scoring techniques are an evaluation on the basis of the severity of typical symptoms.

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In conclusion, developing a criterion based on the composite score of typical reflux symptoms is useful to the diagnosis of GERD. Symptom questionnaire and scoring techniques are an important step in this analysis. For patients with a moderate or severe composite score, the diagnosis of GERD can be made without further tests in most situations. However, 24-h esophageal pH monitoring is still needed in patients with mild and atypical symptoms.

REFERENCES

1 Lim LG, Ho KY. Gastroesophageal reflux disease at the turn of millennium. World J Gastroenterol 2003; 9: 2135-2136
2 Pan GZ, Xu GM, Ke MY, Han SM, Guo HP, Li ZS, Fang XC, Zou DW, Lu SC, Liu J. Epidemiological study of symptomatic gastroesophageal reflux disease in China: Beijing and Shanghai. Chin J Dig Dis 2000; 1: 2-8
3 Kennedy T, Jones R. The prevalence of gastro-oesophageal reflux symptoms in a UK population and the consultation behaviour of patients with these symptoms. Aliment Pharmacol Ther 2000; 14: 1589-1594
4 Locke GR III, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ III. Prevalence and clinical spectrum of gastroesophageal reflux: a population based study in Olmsted County. Gastroenterology 1997; 112: 1448-1456
5 Talley NJ, Zinsmeister AR, Schleck CD, Melton LJ III. Dyspepsia and dyspepsia subgroups: a population-based study. Gastroenterology 1992; 102: 1259-1268
6 Talley NJ, Boyce P, Jones M. Identification of distinct upper and lower gastrointestinal symptom groupings in an urban population. Gut 1998; 42: 690-695
7 Isolauri J, Laippala P. Prevalence of symptoms suggestive of gastro-oesophageal reflux disease in an adult population. Am Med 1995; 27: 67-70
8 Louis E, DeLooze D, Deprez P, Hiele M, Urbain D, Pelckmans P, Deviere J, Deltenre M. Heartburn in Belgium: prevalence, impact on daily life, and utilization of medical resources. Eur J Gastroenterol Hepatol 2002; 14: 279-284
9 Bytzer P, Christensen PB, Damkier P, Vinding K, Seersholm N, Adenocarcinoma of the esophagus and Barrett’s esophagus: a population-based study. Am J Gastroenterol 1999; 94: 86-91
10 Falk GW. Barrett’s esophagus. Gastroenterology 2002; 122: 1569-1591
11 Buttar NS, Wang KK, Leonovich O, Westcott JY, Pacifico RJ, Anderson MA, Krishnadath KK, Lutzke LS, Burgart LJ. Chemoprevention of esophageal adenocarcinoma by COX-2 inhibitors in an animal model of Barrett’s esophagus. Gastroenterology 2002; 122: 1101-1112
12 Shirvani VN, Ouatu-Lascar R, Kaur BS, Omary MB, Triadafilopoulos G. Cyclooxygenase 2 expression in Barrett’s esophagus and adenocarcinoma: Ex vivo induction by bile salts and acid exposure. Gastroenterology 2000; 118: 487-496
13 Sampiner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett’s esophagus. Am J Gastroenterol 1998; 93: 1028-1033
14 Klauser AG, Schindlbeck NE, Muller-Lissner SA. Symptoms in gastro-oesophageal reflux disease. Lancet 1990; 335: 205-208
15 Costantini M, Crookes PF, Bremmer RM, Hoeft SF, Ehsan A, Peters JH, Bremmer CG, DeMeester TR, Calif LA. Value of physiologic assessment of foregut symptoms in a surgical practice. Surgery 1993; 114: 780-787
16 Ho KY, Kang JY, Seow A. Prevalence of gastrointestinal symptoms in a multiracial Asian population, with particular reference to reflux-type symptoms. Ann J Gastroenterol 1998; 93: 1816-1822
17 Grossi L, Cicciaglione AF, Travaglini N, Marzio L. Transient lower esophageal sphincter relaxations and gastroesophageal reflux episodes in healthy subjects and GERD patients during 24 hours. Dig Dis Sci 2001; 46: 815-821
18 Kahrilas PJ, Shi G, Manka M, Joel RH. Increased frequency of transient lower esophageal sphincter relaxation induced by gastric distention in reflux patients with hiatal hernia. Gastroenterology 2000; 118: 688-695
19 Cadiot G, Bruhat A, Rigaud D, Coste T, Vuagnat A, Benyedder Y, Vallot T, Le Guludec D, Mignon M. Multivariate analysis of pathophysiological factors in reflux oesophagitis. Gut 1997; 40: 167-174
20 Ueno M, Hongo M. Clinical significance of 24-hour intrasophageal pH monitoring in GERD patients. Nippon Rinsho 2000; 58: 1818-1822
21 Tefera I, Fein M, Ritter MP, Bremmer CG, Crookes PF, Peters JH, Hagen JA, DeMeester TR. Can the combination of symptoms and endoscopy confirm the presence of gastroesophageal reflux disease? Am Surg 1997; 63: 933-936
22 Colas-Alteg E, Bonaz B, Papillon E, Gueddah N, Rolachon A, Bost R, Fournet J. Relationship between acid reflux episodes and gastroesophageal reflux symptoms is very inconstant. Dig Dis Sci 2002; 47: 645-651
23 Ott DJ, McManus CM, Ledbetter MS, Chen MY, Gelfand DW. Heartburn correlated to 24-hour pH monitoring and radiographic examination of the esophagus. Am J Gastroenterol 1997; 92: 1827-1830
24 Arango L, Angel A, Molina RI, Marquez JR. Comparison between digestive endoscopy and 24-hour esophageal pH monitoring for the diagnosis of gastroesophageal reflux esophagitis: "presentation of 100 cases". Hepatogastroenterology 2000; 47: 174-180
25 Chan CC, Lee CL, Wu CH. Twenty-four-hour ambulatory esophageal pH monitoring, in patients with symptoms of gastroesophageal reflux. J Formos Med Assoc 1997; 96: 874-878
26 Quigley EM. Non-erosive reflux disease: part of the spectrum of gastro-oesophageal reflux disease, a component of functional dyspepsia, or both? Eur J Gastroenterol Hepatol 2001; 13(Suppl 1): S13-18
27 Kauer WK, Peters JH, DeMeester TR, Ireland AP, Bremmer CG, Hagen JA. Mixed reflux of gastric and duodenal juices is more harmful to the esophagus than gastric juice alone. The need for surgical therapy re-emphasized. Ann Surg 1995; 222: 525-531
28 Lin KM, Ueda RK, Hinder RA, Stein HJ, DeMeester TR. Etiology and importance of alkaline esophageal reflux. Am J Gastroenterol 1991; 86: 553-557
29 Vaezi MF, Richter JE. Role of acid and duodenogastroesophageal reflux in gastroesophageal reflux disease. Gastroenterology 1996; 111: 1192-1199

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