J Gastroenterol 2008; 43:798–802
DOI 10.1007/s00535-008-2228-z

Journal of Gastroenterology

Relationship of the frequency scale for symptoms of gastroesophageal reflux disease with endoscopic findings of cardiac sphincter morphology

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Background. Kusano et al. developed a questionnaire for the evaluation of gastroesophageal reflux disease (GERD), the frequency scale for the symptoms of GERD (FSSG). The FSSG is now widely used in Japan. We investigated the relationship between FSSG results and cardiac sphincter endoscopic findings. ***Methods.*** The subjects were 470 patients who responded to the FSSG before undergoing endoscopy. From the FSSG results, we calculated the total, acid reflux, and dysmotility scores. Endoscopic findings were assessed in terms of the anatomic-functional-pathological (AFP) classification as the A factor, or degree and type of hiatal hernia, and the valve factor, or laxity of the cardiac sphincter. The degree of esophagitis was assessed using the modified Los Angeles classification. We investigated correlations between each score and the anatomy of the cardia. ***Results.*** With either definition of esophagitis (grade M or greater, or grade A or greater), the total and acid reflux scores were both significantly higher in the group with reflux esophagitis than in the group without reflux esophagitis. Examination of the relationship between FSSG scores and the A factor revealed no significant differences in the total, acid reflux, or dysmotility scores whether a hiatal hernia was present or absent. Similarly, examination of the valve factor showed no significant difference in any scores between V0 and V1 versus V1 and V2, indicating no correlation between cardiac sphincter laxity and FSSG scores. ***Conclusions.*** The FSSG was useful in determining whether reflux esophagitis is present, but it did not predict the anatomy of the cardia.

Key words: anatomic-functional-pathological classification, frequency scale for the symptoms of gastroesophageal reflux disease, gastroesophageal reflux disease, reflux esophagitis, valve factor

Received: October 4, 2007 / Accepted: June 2, 2008
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Introduction

Gastroesophageal reflux disease (GERD) is a common condition in Western countries,[1–5] and it is attracting increasing attention in Asian countries where it was previously considered uncommon.[6–9] GERD, and in particular erosive GERD, is readily diagnosed endoscopically. Other modalities used in assessing nonerosive GERD (NERD) include pH monitoring, esophageal motility studies, and esophageal sensitivity testing. These tests, however, are invasive and costly and are not suitable for repeated testing. Questionnaires have therefore been developed as a simple, noninvasive, and inexpensive method of identifying GERD patients. In particular, the QUEST questionnaire developed by Dent et al. is used worldwide.[10]

In recent years, the frequency scale for the symptoms of GERD (FSSG), developed by Kusano et al., which concentrates on the frequency of symptoms and not just whether they are present, has gained in popularity in Japan in particular.[11] The FSSG is a questionnaire comprising 12 questions, of which 7 assess acid reflux symptoms and the remaining 5 assess dysmotility-related symptoms.

GERD patients also have a high incidence of morphological and functional abnormalities of the cardiac sphincter region, such as hiatal hernia. Emerenziani et al. stated that patients with hiatal hernia develop GERD symptoms as a consequence of proximal esophageal exposure and reduced acid clearance of gastric acid.[12] Jones et al. reported that hiatal hernia size is a dominant predictive factor for the development of esophagitis.[13] McGouran et al. also pointed out that laxity of the cardiac sphincter is often seen in GERD patients.[14]

With these background factors in mind, the aim of this study was to investigate whether the FSSG can predict cardiac sphincter morphology as identified at esophagogastroduodenoscopy (EGD).

Subjects and methods

Between March 2005 and December 2006, a total of 505 patients with no history of esophageal or gastric surgery underwent EGD. Of these patients, 35 were excluded because of active peptic ulcers. We finally enrolled 470 subjects, all of whom responded to the FSSG before undergoing EGD. Symptoms were most commonly related to GERD, with heartburn, regurgitation, or dysphagia in 58.1% (273/470), gastric or epigastric pain in 35.5% (167/470), and nausea in 16.0% (75/470). On the other hand, 119 subjects (25.3%) underwent EGD for a checkup and were asymptomatic. The subjects comprised 203 males and 267 females, with a mean age of 53.8 ± 12.5 years (range, 14–87 years).

FSSG questionnaire

The FSSG comprises the following 12 questions: (1) Do you get heartburn? (2) Does your stomach get bloated? (3) Does your stomach ever feel heavy after meals? (4) Do you sometimes subconsciously rub your chest with your hand? (5) Do you ever feel sick after meals? (6) Do you get heartburn after meals? (7) Do you have an unusual (e.g., burning) sensation in your throat? (8) Do you feel full while eating meals? (9) Do some things get stuck when you swallow? (10) Do you get a bitter liquid (acid taste) coming up into your throat? (11) Do you burp a lot? (12) Do you get heartburn if you bend over? Subjects answered according to the frequency of their symptoms, scored as follows: never, 0; occasionally, 1; sometimes, 2; often, 3; always, 4. Questions 1, 4, 6, 7, 9, 10, and 12 are the 7 acid reflux-related questions, and questions 2, 3, 5, 8, and 11 are the 5 dysmotility-related questions. The acid reflux score, dysmotility score, and total score (acid reflux score + dysmotility score) were calculated, and a total score of 8 or more was considered to indicate probable GERD. All subjects undergoing EGD were asked to fill in the FSSG questionnaire, and a nurse or doctor checked that no questions were left unanswered.

Endoscopic assessment

EGD was performed by one of two endoscopists who are board certified by the Japan Gastroenterological Endoscopy Society. Esophagitis was graded according to the Los Angeles classification[15] as modified by Hoshihara,[16] in six steps as grade N (normal), grade M (undemarcated mucosal discoloration), and grades A, B, C, and D. Because of the lack of consensus regarding grade M, we conducted this study with reflux esophagitis defined as both grade M or above and as grade A and above.

As part of the assessment of the anatomy of the cardia, the presence, type, and degree of hiatal hernia were graded as the A factor using the anatomic-functional-pathological (AFP) classification proposed by the International Society of Diseases of the Esophagus (ISDE).[17] This classification comprises A0, no hiatal hernia; A1, <3 cm sliding hiatal hernia; A2, ⩾3 cm sliding hiatal hernia; and A3, paraesophageal or mixed-type hiatal hernia. Laxity of the cardiac sphincter was assessed in terms of the valve factor proposed by Ismail et al.[18] In other words, during EGD, the scope was reversed on itself within the stomach to look up the cardia and the findings were classified as follows: no hiatal hernia present, and the cardiac sphincter did not open after sufficient dilatation of the fornix by insufflation of air, V0; hiatal hernia present, but the cardiac sphincter did not open after sufficient dilatation of the fornix by insufflation of air, V1; no hiatal hernia present, but the cardiac sphincter opened after sufficient dilatation of the fornix by insufflation of air, V2; hiatal hernia present, and the cardiac sphincter opened after sufficient dilatation of the fornix by insufflation of air, V3.

Statistical analyses

Data are presented as median (minimum, maximum). All data were entered into Statview version 5.0J (SAS Institute Japan, Tokyo, Japan). The data were not normally distributed, so that the Kruskal–Wallis analysis of variance was used to compare the three groups. After that, statistical analysis was performed using the Mann–Whitney *U* test for comparison of two groups. A *P* value less than 0.05 was considered significant.

Results

Subject characteristics

Characteristics of the 470 subjects are shown in Table 1. Using the modified Los Angeles classification, wherein esophagitis was defined as grade M or greater, esophagitis was seen in 161 subjects (34.3%). When esophagitis was defined as grade A or greater, it was seen in 72 subjects (15.3%). Hiatal hernia (other than A0) was identified in 210 subjects (44.7%). Cardiac laxity (V2 or V3) was identified in 218 subjects (46.4%).

Sensitivity, specificity, and accuracy

With reflux esophagitis is defined as grade M or greater, a cutoff value of 8 points for the FSSG total score pro-

Table 1. Subject characteristics

Sex (male/female)	203/267
Age (years)	53.8 ± 12.5
Body mass index (BMI, kg/m^2)	22.4 ± 2.6
A-factor (A0/A1/A2/A3)	260/202/8/0
V-factor (V0/V1/V2/V3)	224/28/36/182
Los Angeles classification (grade N/M/A/B/C/D)	309/89/62/7/3/0
Caffeine intake (patients)	20
Concomitant disease (patients)	
Hypertension	38
Hyperlipemia	14
Diabetes mellitus	5
Cholelithiasis	2
Hyperuricacidemia	3
Osteoporosis	2
Rheumatoid arthritis	1
Parkinson disease	1

vided a sensitivity of 57.0%, specificity of 59.2%, and accuracy of 58.3%. Defining reflux esophagitis as grade A or greater provided a sensitivity of 57.0%, specificity of 55.8%, and accuracy of 56.0%.

Relationship between reflux esophagitis and FSSG scores

Defining reflux esophagitis as grade M or greater, the total and acid reflux scores were both significantly higher in the group with reflux esophagitis than in the group without reflux esophagitis ($P = 0.0011$ and 0.0004, respectively), although the difference between dysmotility scores was not significant ($P = 0.0551$). When reflux esophagitis was defined as grade A or greater, similarly the total and acid reflux scores were both significantly higher in the group with reflux esophagitis than in the group without reflux esophagitis ($P = 0.0233$, 0.0024), and the difference between dysmotility scores was not significant ($P = 0.5127$).

Furthermore, the patients were classified into the following three groups by the degree of esophagitis: grade N, grade M, and grades A–D. As the esophagitis became worse, both the total scores and the acid reflux scores were significantly higher ($P = 0.0043$, 0.0009, respectively), but there were no significant differences with the dysmotility scores ($P = 0.1337$).

The total and acid scores were both significantly higher in the grade M patients than in the grade N patients ($P = 0.0164$ and 0.0261, respectively). Similarly, the total and acid scores were both significantly higher in the grade A–D patients than in the grade N patients ($P = 0.0067$ and 0.0006, respectively); however, significant differences were not observed between grade M and grade A–D patients ($P = 0.6754$ and 0.2458, respectively) (Table 2).

Table 2. Relationship between degree of esophagitis and frequency scale for evaluation of gastroesophageal reflux disease (FSSG) (grade N vs. grade M vs. grade A–D)

	Scores		
	Total*	Acid reflux***	Dysmotility^{ns}
Grade N ($n = 309$)	5 (0, 34)	3 (0, 20)	3 (0, 19)
Grade M ($n = 89$)	8 (0, 36)**	4 (0, 16)**	4 (0, 20)
Grade A–D ($n = 72$)	9 (0, 34)†	4 (0, 18)†	3 (0, 16)

* $P = 0.0043$; ** $P < 0.05$ vs. grade N; *** $P = 0.0009$; † $P < 0.01$ vs. grade N
ns, not significant

Table 3. Non-GERD vs. nonerosive GERD (NERD) vs. erosive GERD (grades A–D)

	Scores		
	Total*	Acid reflux***	Dysmotility††
Non-GERD ($n = 191$)	2 (0, 22)	0 (0, 10)	2 (0, 14)
NERD ($n = 207$)	11 (1, 36)**,†	5 (1, 20)**	5 (0, 20)**,†
Erosive GERD ($n = 72$)	9 (0, 34)**	4 (0, 18)**	3 (0, 16)**

* $P < 0.0001$; ** $P < 0.0001$ vs. non-GERD; *** $P < 0.0001$; † $P < 0.05$ vs. erosive GERD; †† $P < 0.0001$

Non-GERD versus NERD versus erosive GERD

We defined the patients with grades A–D as having erosive GERD, the patients of grades N and M with the symptom of heartburn as NERD, and the patients of grades N and M without heartburn symptom as non-GERD. The total, acid reflux and dysmotility scores significantly differed among the three groups ($P < 0.0001$ each).

All scores were significantly higher in the NERD patients than in the non-GERD patients ($P < 0.0001$ each). Similarly, all scores were significantly higher in the erosive GERD patients than in the non-GERD patients ($P < 0.0001$ each). The total and dysmotility scores were both significantly higher in the NERD patients than in the erosive GERD patients ($P = 0.0275$ and 0.0077, respectively), although the difference between acid reflux scores was not significant ($P = 0.1122$) (Table 3).

Especially, NERD patients had the highest score in these three groups. The dysmotility score of NERD patients was significantly higher than that of non-GERD and erosive GERD patients.

Table 4. Relationship between hiatal hernia and FSSG (A0 vs. A1–A3)

	Scores					
	Total		Acid reflux		Dysmotility	
A0 (n = 260)	7 (0, 34)	ns	3 (0, 20)	ns	3 (0, 19)	ns
A1–A3 (n = 210)	6.5 (0, 36)		3 (0, 18)		3 (0, 20)	

ns, not significant

Table 5. Relationship between value factor and FSSG (V0, V1 vs. V2, V3)

	Scores					
	Total		Acid reflux		Dysmotility	
V0, V1 (n = 252)	6 (0, 34)	ns	3 (0, 20)	ns	3 (0, 18)	ns
V2, V3 (n = 218)	7 (0, 36)		3 (0, 18)		3 (0, 20)	

ns, not significant

Relationship between hiatal hernia and FSSG scores

No significant difference was seen in the FSSG total, acid reflux, or dysmotility scores according to hiatal hernia status (A0 vs. A1, A2, A3) (P = 0.6367, P = 0.7735, P = 0.1874, respectively) (Table 4).

Relationship between valve factor and FSSG scores

No significant difference was seen in the FSSG total, acid reflux, or dysmotility scores between the group without cardiac sphincter laxity (V0, V1) and the group with cardiac sphincter laxity (V1, V2) (P = 0.4388, P = 0.262, P = 0.9056, respectively) (Table 5).

Discussion

GERD is diagnosed using EGD and 24-h esophageal pH monitoring. The latter allows objective analysis of acid reflux into the esophagus, with many studies confirming its usefulness. Nevertheless, 24-h pH monitoring is associated with problems such as the required length of time and the necessity to insert a catheter transnasally, although it was of narrow caliber. EGD can be readily performed, and is useful in diagnosing erosive GERD, but it is not suitable for the diagnosis of NERD.

With these considerations in mind, the proton pump inhibitor (PPI) test is a simple and cost-effective means of confirming the presence of GERD, and questionnaires have also been developed to pick up cases of GERD. The QUEST questionnaire developed by Dent et al. is particularly widely used.[10] However, QUEST is not without problems; with a cutoff of 4 points, it will identify a patient with only heartburn symptoms as GERD positive. Accordingly, Kusano et al. developed the FSSG questionnaire.[11] The FSSG has largely replaced the QUEST questionnaire in Japan, and it is widely used and studied. The FSSG comprises acid reflux-related questions and dysmotility-related questions and also assesses symptom frequency.

GERD in Asian patients is usually mild, and esophagitis with mucosal breaks is reported to be uncommon.[19] Mild disease is common, with symptomatic GERD making up the majority of cases in Japanese patients.[20] Our results are consistent with previous reports, with higher scores for sensitivity, specificity, and accuracy for the FSSG when esophagitis was defined as grade M or above than for grade A and above.

Esophageal hiatal hernia is considered an important etiological factor for GERD.[21] In general, hiatal hernia is thought to be uncommon in patients with symptomatic GERD.[22] We have previously reported, however, that morphological abnormalities of the cardiac sphincter, namely, hiatal hernia or chalasia (V factor V2 or V3), are present in the majority of Japanese patients with symptomatic GERD.[23] In this study, we investigated the relationship between FSSG results and the anatomy of the cardia as observed endoscopically. We found no significant differences between total, acid reflux, or dysmotility scores according to the A factor (presence or absence of hiatal hernia) or V factor (presence or absence of chalasia).

A definite esophageal hiatal hernia (A2 or A3) was identified in only eight subjects (1.7%), and most of the subjects were A1 or A0. It would therefore appear that a small hiatal hernia, graded as A1, would not be reflected in the FSSG score. Against expectations, the V factor also had no discernible effect on FSSG scores. Unless the intragastric pressure exceeds a certain level (insufflation of approximately 500 ml air), the V factor does not become positive (V2 or V3). It seems likely that, with regular eating and drinking habits, changes in

intragastric pressure that will cause symptoms do not occur. This may be one of the reasons why a correlation was not seen between the V factor and the FSSG score. Whether the definition of reflux esophagitis included grade M or not, the total and acid reflux scores were both significantly higher in the group with reflux esophagitis than in the group without reflux esophagitis, in accordance with earlier reports.[2]

In addition, we classified patients into three groups: grades N, M, and A–D by the degrees of esophagitis. As the esophagitis became worse, both the total scores and acid reflux scores became significantly higher. We think that these results are similar to previous reports.

All scores significantly differed among the non-GERD, NERD, and erosive GERD groups. Especially, the dysmotility score of NERD patients was significantly higher than that of non-GERD and erosive GERD patients. These results suggest that the dysmotility of the upper gastrointestinal tract strongly influences the symptoms of affected NERD patients.

We conducted this study under the assumption that the FSSG questionnaire would be a particularly useful diagnostic tool if it could predict the anatomical or functional status of the cardia. Our results indicated, however, that although the FSSG is useful in determining the presence of reflux esophagitis, it does not correlate cardiac sphincter morphology, such as abnormalities of the cardia, or problems such as an esophageal hiatal hernia or chalasia. In addition, cardiac sphincter morphology does not represent GERD symptoms.

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