

EDITORIAL

Questionnaires for the diagnosis of gastroesophageal reflux disease: are they really useful for a diagnostic goal?

Gastroesophageal reflux disease (GERD) is a major medical complaint both in primary care and gastroenterology clinics. This is partly due to the condition's high prevalence, which is estimated to be 10-20% in developed countries (1). Its initial diagnosis, however, remains controversial.

The Montreal definition of GERD is widely accepted, and both heartburn and regurgitation are therein considered as the syndrome's typical symptoms (2). However, in the DIAMOND study only 49% of patients with GERD surprisingly report these symptoms as major causes of disability (40% heartburn, 9% regurgitation) (3). Furthermore, these symptoms are not highly sensitive or specific to predict the presence of injury during endoscopy, and may also be present in other non-GERD conditions such as achalasia or eosinophilic esophagitis (4). These limitations require that tests such as endoscopy and pH-monitoring be used in their various modalities for diagnosis. The latter test (with or without impedanciometry, wireless pH-monitoring) remains the gold standard for the diagnosis of this condition in the absence of endoscopic lesion (5). Given the high prevalence of GERD, the use of diagnostic techniques, besides other factors such as treatments and impact on quality of life, renders the financial burden of this condition high (6).

From all the above, GERD diagnosis has been attempted by other means, including the proton-pump inhibitor (PPI) test and the use of specific questionnaires.

As regards the former, it is poorly defined in the literature; some studies suggest the use of dual PPI doses for 14-28 days whereas others use a single or dual PPI dose for 7, 14 or 28 days (7). What should be considered a therapeutic response is also poorly established (8). Acceptable sensitivity but low specificity have been reported for this test, which has not proven its ability to discriminate between patients with and without GERD; hence, it may wrongly classify some patients as having GERD in the absence of abnormal reflux during pH-monitoring, as occurs in patients with functional heartburn (9,10).

Regarding questionnaires, a wide variety are available that significantly differ in characteristics, design, and goals, according to the aspect of GERD to be tested (11). In those with a diagnostic goal, some have not been compared to other diagnostic tests such as endoscopy or pH-monitoring (12,13), or have shown limited sensitivity and specificity (14,15).

A validated questionnaire most commonly used for the diagnosis of GERD is the Gastroesophageal Reflux Disease Questionnaire (GerdQ), which was developed as part of the DIAMOND study; with this test, some upper digestive complaints were correlated to GERD markers (3). This questionnaire assesses six factors for a final score, with 65% sensitivity and 71% specificity (16).

This questionnaire has been compared in several studies with objective diagnostic tests such as pH-monitoring and/or endoscopy (Table I). Lacy et al. (17) also performed this comparison with prolonged wireless pH-monitoring studies for up to 48 hours, and

Table I. Diagnostic usefulness of the GerdQ and GSFQ tests

	Questionnaire	Gold standard	Cutoff	SS	SP	AUROC	PPV	NPV
Jones (16)	GerdQ	pH-monitoring/endoscopy	≥ 8	64.6%	71.4%			
Lacy (17)	GerdQ	Wireless pH-monitoring (48 hrs)	≥ 8 OCP > 10	71% 43%	41% 75%	56% 61%*		
Jonasson (19)	GerdQ	Endoscopy	≥ 9	66%	64%	70%	92%	22%
Zavala-Gonzales (21)	GerdQ	Endoscopy and/or pH-monitoring	≥ 8	71.6%	72.2%	73.8%	86.5%	50.5%
Suzuki (20)	GerdQ	Endoscopy (esophagitis)	≥ 8	34.3%	82.5%	58%**	20.3%	90.6%
Bai (22)	GerdQ (heartburn + regurgitation)	Endoscopy (esophagitis)	≥ 8	44%	75%		27%	86%
Teruel (25)	GSFQ	pH-monitoring	≥ 8 OCP ≥ 13	36.6% 39.8%	77.5% 82.5%	53.9% 59%		

GerdQ: Gastroesophageal Reflux Disease Questionnaire; GSFQ: Gastrointestinal Short Form Questionnaire; OCP: Optimal cutoff point; SS: Sensitivity; SP: Specificity; AUROC: Area under the ROC curve; PPV: Positive predictive value; NPV: Negative predictive value; *p < 0.01; **p = 0.02.

reported that high scores increased the probability of GERD in patients. However, the GerdQ with the cutoff point used in the DIAMOND study (score ≥ 8) had modest sensitivity and specificity (66% and 48%, respectively). Sensitivity improved when symptom analysis was included in addition to abnormal acid exposure (77%), and when patients were off PPIs (71%) (17). This questionnaire, however, has proven to be useful as initial diagnostic approach for primary care, representing also a healthcare cost-saving strategy (18,19).

Also, this ≥ 8 cutoff value has been confirmed by other studies as the one providing the best sensitivity and specificity in the identification of esophagitis (20) and the exclusion of functional heartburn (21). Furthermore, it should be noted that a low score does not rule out esophagitis and also does not fully discriminate the potential for other conditions, including tumors with no associated alarm symptoms (22).

Another commonly used questionnaire is the Gastrointestinal Short Form Questionnaire (GSFQ) (23), an easy-to-fill tool that has been validated in Spanish (24). This is a specific questionnaire developed to assess the frequency of GERD symptoms and their impact on quality of life. It comprises of 6 items, 4 of which may be answered using an ordinal scale. The first 4 questions explore the frequency of GERD symptoms during the last 7 days, and one of them refers to GERD-related limitations on food. The last two questions determine the number of days GERD symptoms interfered in daily activities and sleep during the previous week.

This questionnaire possesses adequate psychometric characteristics, is sensitive to changes induced by therapy, and significantly correlates to quality of life as measured by generic questionnaires (24). To date, no studies have compared it to other specific diagnostic tests such as outpatient pH-monitoring.

The study by Teruel et al. (25) assesses the sensitivity and specificity of this questionnaire using outpatient pH-monitoring. They find the optimal cutoff point to be ≥ 13 with a sensitivity of 40.0% (95% CI: 30.3-50.3%) and specificity of 71.2% (95% CI: 56.9-82.9%). Therefore, the questionnaire has low sensitivity and modest specificity when compared to pH-monitoring. The significance of these results is that, when compared to the extant gold-standard for the study of GERD, the questionnaire does not seem a valid diagnostic option for specialist care.

Questionnaires no doubt represent a useful tool for the initial diagnostic approach in the absence of alarm symptoms, and they may be used whether alone or concurrently with other test, on an individual basis.

They may also be useful for the monitoring of therapy response, particularly in the primary care setting (18).

Furthermore, up to 50% of therapy failures in the setting of non-erosive GERD are related to motor disorders amenable to high-resolution manometry. Therefore, while questionnaires may be useful for therapy assessment, we should take into account the response to the treatment whether is ineffective or incomplete, then the diagnosis with tests such as endoscopy and/or pH-monitoring would be more appropriate.

In summary, a wide variety of questionnaires are available for the study of GERD, and their selection depends on the aspect to be assessed: diagnosis, therapeutic response, or quality of life. While they are useful as initial diagnostic approach, none of them can be used as single diagnostic test for GERD.

Constanza Ciriza-de-los-Ríos

Department of Digestive Diseases. Hospital Universitario 12 de Octubre. Madrid, Spain

REFERENCES

- Dent J, El-Serag H, Wallander MA, et al. Epidemiology of gastroesophageal reflux disease: A systematic review. *Gut* 2005;54:710-7. DOI: 10.1136/gut.2004.051821
- Vakil N, Van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: A global evidence-based consensus. *Am J Gastroenterol* 2006;101:1900-20;quiz 43. DOI: 10.1111/j.1572-0241.2006.00630.x
- Dent J, Vakil N, Jones R, et al. Accuracy of the diagnosis of GORD by questionnaire, physicians and a trial of proton pump inhibitor treatment: The Diamond Study. *Gut* 2010;59:714-21. DOI: 10.1136/gut.2009.200063
- Tsuboi K, Hoshino M, Srinivasan A, et al. Insights gained from symptom evaluation of esophageal motility disorders: A review of 4,215 patients. *Digestion* 2012;85:236-42. DOI: 10.1159/000336072
- Vakil N. The initial diagnosis of GERD. *Best Pract Res Clin Gastroenterol* 2013;27:365-71. DOI: 10.1016/j.bpg.2013.06.007
- Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology* 2012;143:1179-87e1-3. DOI: 10.1053/j.gastro.2012.08.002
- Numans ME, Lau J, De Wit NJ, et al. Short-term treatment with proton-pump inhibitors as a test for gastroesophageal reflux disease: A meta-analysis of diagnostic test characteristics. *Ann Intern Med* 2004;140:518-27. DOI: 10.7326/0003-4819-140-7-200404060-00011
- Numans ME. The use of proton pump inhibitors as a diagnostic test for gastroesophageal reflux disease. *Arch Intern Med* 2006;166:247-8. DOI: 10.1001/archinte.166.2.247-b
- Ciriza-de-los-Ríos C, García-Menéndez L, Díez-Hernández A, et al. Motility abnormalities in esophageal body in GERD: Are they truly related to reflux? *J Clin Gastroenterol* 2005;39:220-3.
- Bytzer P, Jones R, Vakil N, et al. Limited ability of the proton-pump inhibitor test to identify patients with gastroesophageal reflux disease. *Clin Gastroenterol Hepatol* 2012;10:1360-6. DOI: 10.1016/j.cgh.2012.06.030

11. Bolier EA, Kessing BF, Smout AJ, et al. Systematic review: Questionnaires for assessment of gastroesophageal reflux disease. *Dis Esophagus* 2015;28:105-20. DOI: 10.1111/dote.12163
12. Locke GR, Talley NJ, Weaver AL, et al. A new questionnaire for gastroesophageal reflux disease. *Mayo Clin Proc* 1994;69:539-47. DOI: 10.1016/S0025-6196(12)62245-9
13. Moreno Elola-Olaso C, Rey E, Rodríguez-Artalejo F, et al. Adaptation and validation of a gastroesophageal reflux questionnaire for use on a Spanish population. *Rev Esp Enferm Dig* 2002;94:745-58.
14. Horowitz N, Moshkowitz M, Halpern Z, et al. Applying data mining techniques in the development of a diagnostics questionnaire for GERD. *Dig Dis Sci* 2007;52:1871-8. DOI: 10.1007/s10620-006-9202-5
15. Ho KY, Gwee KA, Khor JL, et al. Validation of a graded response questionnaire for the diagnosis of gastroesophageal reflux disease in an Asian primary care population. *J Clin Gastroenterol* 2008;42:680-6. DOI: 10.1097/MCG.0b013e3180653613
16. Jones R, Junghard O, Dent J, et al. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. *Aliment Pharmacol Ther* 2009;30:1030-8. DOI: 10.1111/j.1365-2036.2009.04142.x
17. Lacy BE, Chehade R, Crowell MD. A prospective study to compare a symptom-based reflux disease questionnaire to 48-h wireless pH monitoring for the identification of gastroesophageal reflux (revised 2-26-11). *Am J Gastroenterol* 2011;106:1604-11. DOI: 10.1038/ajg.2011.180
18. Jonasson C, Moum B, Bang C, et al. Randomized clinical trial: A comparison between a GerdQ-based algorithm and an endoscopy-based approach for the diagnosis and initial treatment of GERD. *Aliment Pharmacol Ther* 2012;35:1290-300. DOI: 10.1111/j.1365-2036.2012.05092.x
19. Jonasson C, Wernersson B, Hoff DA, et al. Validation of the GerdQ questionnaire for the diagnosis of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2013;37:564-72. DOI: 10.1111/apt.12204
20. Suzuki H, Matsuzaki J, Okada S, et al. Validation of the GerdQ questionnaire for the management of gastro-oesophageal reflux disease in Japan. *United European Gastroenterol J* 2013;1:175-83. DOI: 10.1177/2050640613485238
21. Zavala-Gonzales MA, Azamar-Jacome AA, Meixueiro-Daza A, et al. Validation and diagnostic usefulness of gastroesophageal reflux disease questionnaire in a primary care level in Mexico. *J Neurogastroenterol Motil* 2014;20:475-82. DOI: 10.5056/jnm14014
22. Bai Y, Du Y, Zou D, et al. Gastroesophageal Reflux Disease Questionnaire (GerdQ) in real-world practice: A national multicenter survey on 8,065 patients. *J Gastroenterol Hepatol* 2013;28:626-31. DOI: 10.1111/jgh.12125
23. Pare P, Meyer F, Armstrong D, et al. Validation of the GSFQ, a self-administered symptom frequency questionnaire for patients with gastroesophageal reflux disease. *Can J Gastroenterol* 2003;17:307-12.
24. Ruiz-Díaz MA, Suárez-Parga JM, Pardo-Merino A, et al. Cultural adaptation to Spanish and validation of the Gastrointestinal Short Form Questionnaire. *Gastroenterol Hepatol* 2009;32:9-21.
25. Teruel-Sánchez-Vegazo C, Faro-Leal V, Muriel-García A, et al. Sensitivity and specificity of the Gastrointestinal Short Form Questionnaire in diagnosis of gastroesophageal reflux disease. *Rev Esp Enferm Dig* 2016;108:174-80. DOI: 10.17235/reed.2016.4082/2015