New Questionnaire for Eosinophilic Esophagitis: Will It Measure What We Want?

See "Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis," by Schoepfer AM, Straumann A, Panczak R, et al, on page 1255.

A standardized and validated patient-reported outcome (PRO) instrument assessing symptom severity in patients with eosinophilic esophagitis (EoE) is needed for clinically relevant medical experiments in clinical trials and observational studies. In this issue of *Gastroenterology*, Schoepfer et al[1] and a multidiscipline team of Swiss and American EoE experts have hopefully accomplished this task. They call their instrument the Adult Eosinophilic Esophagitis Activity Index PRO. Generating patient information from open-ended patient surveys, focus groups and semi-structured patient interviews, the PRO instrument contains 5 domains: Sociodemographic, symptoms independent of eating, symptoms related to eating, comorbidities, and medication use. An-8 food consistency panel was developed with illustrations, which can be exchanged for those with unusual diets (vegetarians, gluten-free or elimination diets):

1. Solid meat
2. Soft foods
3. Dry or sticky rice
4. Ground meat
5. Fresh white untoasted bread
6. Grits, porridge, rice pudding
7. Raw fibrous vegetables
8. French fries.

A 7-day recall period was chosen. The instrument takes approximately 8 minutes to administer, was easy to comprehend and complete, and predicted 67% of the variability in disease severity based on a Patient Global Assessment of EoE severity using an 11-point Likert scale.

The lack of reliable PRO instruments has plagued drug treatment outcome studies in EoE, especially for adult patients. The Straumann Dysphagia Index does not assess specifically dysphagia caused by various food textures nor does it take into consideration behavioral adaptation to eating these foods.[2] The Mayo Dysphagia Questionnaire 30-Day version, popular in US studies,[3] was developed for assessing dysphagia owing to various esophageal diseases, but not for EoE specifically. Dellon et al[4] developed a dysphagic symptom questionnaire, a 3-item electronic PRO administered daily to assess the frequency of dysphagia caused by eating "solid foods" and strategies to relieve dysphagia symptoms. However, the terminology for solid food was vague and did not evaluate various food groups. As a result, the swallowing measures are not interchangeable and discordant results have been reported in adults and children with mucosal eosinophilia improving, but dysphagia scores not showing significant changes.[3,5]

The developers of this new questionnaire have done a particularly commendable job in addressing the emotional factors involved in dysphagia. The severity of the disease causes patients in an unpredictable, individual manner to avoid certain food types and adapt behavioral strategies to minimize their symptoms and socially embarrassing moments (ie, food impaction, rushing to leave the table). The visual illustration of the 8 food consistencies is a "hypothetical test meal" that does not require a test kitchen, individual grocery list, or fear of food impactions. Behavioral adaptation strategies are assessed for each food group, including total avoidance, modification of the food (ie, put in a blender, cut up into tiny pieces, dunk in water, mash up), and slower eating compared with others at the table.

Unfortunately, the pathophysiologic mechanisms leading to dysphagia are just as complex as the emotional factors (Figure 1). The inciting event is the mucosal inflammation initiated by the eosinophils and their mediators. However, the degree of mucosal eosinophilia does not seem to correlate with the degree of dysphagia.[3–6] This confirms that other factors, such as dysmotility and/or mechanical outflow obstruction owing to subepithelial fibrosis, are important contributors to the complaints of dysphagia.[7–10] In the latter mechanism, this may range from subtle decrease in esophageal distensibility and compliance to esophageal strictures and small caliber esophagus, which sometimes can be missed at endoscopy. Furthermore, the contributions of each varies in the individual patient and may be unknown in some patients if only simple endoscopy with biopsies is the sole criteria for entrance into a study. More important, most intervention studies (medications or esophageal dilations) only address one of these mechanisms. For example, esophageal dilation improves dysphagia for on average 2 years despite not changing the degree of mucosal eosinophilia in EoE patients, primarily with the fibrostenotic phenotypes.[11] On the other hand, patients with the inflammatory phenotype will do well on steroid preparations, but some will have less optimal outcomes because of unrecognized motility disturbances or esophageal strictures.[3,5]

Now, the key question is will this new questionnaire be responsive to treatment intervention trials for old and new drugs allowing us to get much-needed US Food and Drug Administration–approved therapies for EoE? This clinical investigator hopes so, and greatly appreciates the large amount of time spent in developing the Adult Eosinophilic Esophagitis Activity Index PRO. However, "time will tell" and "patients can

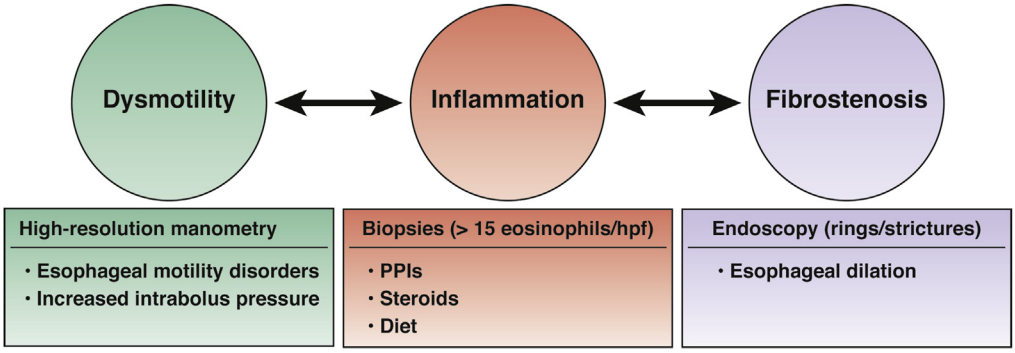

Figure 1. Mechanical factors contributing to dysphagia and eosinophilic esophagitis. PPI, proton pump inhibitor.

be very unpredictable." I have observed patients who after dilation to 17-18 mm still are fearful of food impaction and stay on softer foods, avoiding meats and fibrous vegetables. Furthermore, patients want to please us in clinical trials and may overestimate their improvement in eating habits. This is the advantage of observing the patient while eating a test meal containing all 8 food groups. This possibly could be circumvented by getting validation of the eating habits and behavioral accommodation from the patient's eating partner (ie, spouse, parent, significant other). Finally, the sensitivity of the test questionnaire to changes in mild EoE disease is unknown and may be an issue, because the inflammatory phenotype has replaced the fibrostenotic phenotype as the most common presentation in adults as well as children.[12]

In conclusion, we now have a simple, easy to administer EoE questionnaire with dietary flexibility that measures all the emotional domains of dysphagia and is accurate in assessing the baseline severity of symptoms. It has not been evaluated and validated in children. How sensitive it will be to measure changes in milder forms of EoE is potentially problematic. In more severe diseases, it will not be a substitute for understanding the mechanical factors contributing to the patient's dysphagia, which may not be addressed with a single drug therapy. Will this "hypothetical test meal" really replace feeding the patient by a trained observer and keep the EoE clinician and investigator "out of the kitchen"? Time and future drug trials will tell.

JOEL E. RICHTER
Department of Medicine
Hugh F. Culverhouse Chair for Esophageal Disorders
Director, Division of Digestive Diseases & Nutrition *and*
Joy McCann Culverhouse
Center for Esophageal and Swallowing Disorders
University of South Florida Morsani College of Medicine
Tampa, Florida

References

1. Schoepfer AM, Straumann A, Panczak R, et al. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. Gastroenterology 2014;147:1255–1266.
2. Straumann A, Conus S, Degen L, et al. Budesonide is effective in adults and adolescents with active eosinophilic esophagitis. Gastroenterology 2010;129:1526–1537.
3. Alexander JA, Jung KW, Arora AS, et al. Swallowed fluticasone improves histologic but not symptom response of adults with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2012;10:742–749.
4. Dellon ES, Irani AM, Hill MR, et al. Development and fielding testing of novel patient-reported outcome measure of dysphagia in patients with eosinophilic esophagitis. Aliment Pharmacol Ther 2013;38:634–642.
5. Pentiuk S, Putnam PE, Collins M, et al. Dissociation between symptoms and histologic severity in pediatric eosinophilic esophagitis. J Pediatr Gastroentol Nutr 2009;48:152–160.
6. Dellon ES. Diagnosis and management of eosinophilic esophagitis. Clin Gastroenterol Hepatol 2012;10:1066–1078.
7. Dellon ES, Liacouras CA. Advances in clinical management of eosinophilic esophagitis. Gastroenterology 2014;147:1238–1254.
8. Roman S, Hirano I, Kwiatek MA, et al. Manometric features of eosinophilic esophagitis in esophageal pressure topography. Neurogastroenterol Motil 2011;23:208–215.
9. Schoepfer AM, Safroneeva E, Bussman C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation, in a time-dependent manner. Gastroenterology 2013;145:1230–1236.
10. Kwiatek MA, Hirano I, Kahrilas PJ, et al. Mechanical properties of the esophagus in eosinophilic esophagitis. Gastroenterology 2011;140:82–90.
11. Bohm ME, Richter JE. Review article: oesopheal dilation in adults with eosinophilic esophagitis. Aliment Pharmacol Ther 2011;37:748–757.
12. Dellon ES, Kim HP, Sperry SC, et al. A phenotype analysis shows that eosinophilic esophagitis is a progressive fibrostenotic disease. Gastrointest Endosc 2014;79:577–585.

Reprint requests
Address requests for reprints to: Joel E. Richter, MD, Professor of Medicine, Hugh F. Culverhouse Chair for Esophageal Disorders, Director, Division of Digestive Diseases & Nutrition, Director, Joy McCann Culverhouse, Center for Esophageal and Swallowing Disorders, University of South Florida Morsani College of Medicine, 12901 Bruce B. Downs Boulevard, MDC 72, Tampa, Florida 33624. e-mail: jrichte1@health.usf.edu.

Conflicts of interest
The author discloses no conflicts.

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