



Published in final edited form as:

Gastrointest Endosc. 2016 February ; 83(2): 307–308. doi:10.1016/j.gie.2015.07.006.

Eosinophilic Esophagitis: Search for Non-Invasive Techniques for Long-Term Monitoring

Abhishek Watts, M.D.¹, Jeffrey A. Alexander, M.D.², and Sandeep K. Gupta, M.D.¹

¹Indiana University School of Medicine, Department of Pediatric Gastroenterology, Hepatology and Nutrition

²Mayo Clinic, Department of Gastroenterology and Hepatology

Eosinophilic esophagitis (EoE) is an immune mediated disease characterized clinically by symptoms of esophageal dysfunction and histologically by a marked eosinophilic infiltrate of the esophageal epithelium in the absence of other causes of esophageal eosinophilia. EoE became increasingly recognized in the pediatric population in the mid-1990s, and thereafter in the adult patients. Over time, there has been an increase in awareness and possibly prevalence and incidence of EoE.[1, 2] Currently, the most reliable and objective method to diagnose EoE and/or assess disease status is via performing esophagogastroduodenoscopy (EGD) with biopsies, and patients could undergo multiple EGDs in a relatively short span of disease duration. Normal endoscopic appearance of mucosa does not rule out EoE.

Not only are repeated EGDs invasive, but also require some level of sedation which in the pediatric population often translates into general anesthesia. This leads to involvement of an anesthesiologist, and use of costly facilities such as operating room, resulting in significant health-care costs. Children may experience negative health-related quality of life (HRQoL) due to persistent symptoms and repeated procedures.[3] As such, it is imperative to look for alternate and newer methods which would be accurate, safe, comprehensive and less expensive for monitoring EoE.

Several, potentially less-invasive, techniques are being studied for monitoring EoE disease activity. Fractionated exhaled nitric oxide (FeNO) has been used to assess eosinophil-predominant asthma and EoE. Leung et al[4] measured FeNO in nonasthmatic subjects with active esophagitis before and after treatment with topical steroids. FeNO levels declined post treatment. Subbarao et al [5] prospectively measured serum IL-5, serum eosinophil-derived neurotoxin (EDN), and stool EDN in children with EoE and controls at multiple time-points. Serum EDN levels were significantly higher in subjects with active EoE than in controls or those in remission. Esophageal string test involves collection of esophageal luminal secretions by a string that unravels after a weighted gelatin capsule is swallowed. Preliminary data suggests correlation between disease activity and levels of eosinophil derived granule proteins captured on the string. Another ingestible gelatin capsule, Cytosponge, contains a compressed mesh attached to a string that collects esophageal

mucosal secretions. Katzka et al [6] showed in a pilot study that the sponge is safe and accurate, compared to endoscopic biopsy, in assessing esophageal eosinophilia. Patients with active EoE were identified with 83% sensitivity, and (Cytosponge) was preferred over sedated EGD by all patients studied. The study is promising and if validated on a large patient population, might very well become the new method to monitor EoE in adult population. The third capsule based test uses a high-speed fiber based reflectance confocal microscopy technique termed Spectrally Encoded Confocal Microscopy (SECM). Its images correlate well, with high sensitivity and specificity, with results obtained by conventional histology.[7] The EndoFLIP system uses impedance planimetry to measure esophageal distension which is reduced in patients with EoE compared to the controls.[8] This test however, may ignore regional variation along the esophagus and is somewhat invasive. Microarray technology has been harnessed as in a molecular EoE Diagnostic Panel built on Taqman-qPCR based low density array system. Its limitations would be turnaround time, technical complexity of the messenger RNA microarray, and potential costs.[9] Many of these technologies are not commercially available; hence it is difficult to predict the economic burden these will have on the patient and the health care system.

In the current issue of the *Journal*, the Colorado group reports on a prospective study, wherein unsedated transnasal endoscopies (TNE) with biopsies were performed to monitor EoE in 21 children.[10] Authors provide a single institution experience with data on important determinants such as cost, safety and efficacy. Three proximal and three distal esophageal mucosal biopsies were obtained with biopsy surface area comparable to biopsies with standard EGD. No serious adverse events related to the procedure were reported. The authors report high procedure acceptance rates where all parents and 76.2% of subjects would undergo the TNE again over traditional EGD. The charges associated with TNE at study site were 60.1% less than prior EGD with biopsies. This study is promising and opens doors to newer, less invasive methods to monitor EoE. It provides encouraging preliminary data, and should prompt further study with aim of validating the preliminary results. While TNE is not a non-invasive test, and some limitations include limited endoscopic and histological evaluation of gastric and duodenal mucosa, and additional training, albeit of a short duration, is required of gastroenterologists desiring to perform TNE. Some other unanswered questions are about the size of biopsy samples. While authors report that that their sample size was similar to that obtained during standard EGD, this needs further validation especially as EoE can be a patchy disease. The other concern which can be better addressed in a multicenter study is of the patient acceptance rate. There is a potential for patient selection bias in a single center study such as seen in a large adult study where TNE was declined by half of the patients.[11] In our clinical and research experience the procedure is well tolerated by most but not all patients; 80% of patients undergoing TNE are willing to undergo the procedure again.

In conclusion, unsedated TNE has opened the vistas of new directions and is among the expanding list of novel techniques for monitoring EoE in both pediatric and adult patients. It is cardinaly important that we continue to search for less invasive techniques. With increasing body of knowledge on EoE and widening pool of researchers, we are hopeful that monitoring of EoE will continue to evolve and grow. We have to tread yet a few more miles, but the sanguine hope is that we will definitely get there... sooner than tomorrow.

Acronyms

EoE	Eosinophilic esophagitis
EGD	Esophagogastroduodenoscopy
HRQoL	Health-related quality of life
FeNO	Fractionated exhaled nitric oxide
EDN	Serum eosinophil-derived neurotoxin
SECM	Spectrally Encoded Confocal Microscopy
TNE	Transnasal endoscopy

References

1. Dellon ES, et al. Prevalence of eosinophilic esophagitis in the United States. *Clin Gastroenterol Hepatol.* 2014; 12(4):589–96. [PubMed: 24035773]
2. Karkos PD, et al. Eosinophilic esophagitis for the otolaryngologist. *Int J Otolaryngol.* 2012; 181402(10):15.
3. Lynch MK, et al. Topical Review: Eosinophilic Esophagitis in Children: Implications for Health-Related Quality of Life and Potential Avenues for Future Research. *J Pediatr Psychol.* 2015 Apr 3. pii: jsv032.
4. Leung J, et al. Assessment of fractionated exhaled nitric oxide as a biomarker for the treatment of eosinophilic esophagitis. *Allergy Asthma Proc.* 2012; 33(6):519–24. [PubMed: 23394511]
5. Subbarao G, et al. Exploring potential noninvasive biomarkers in eosinophilic esophagitis in children. *J Pediatr Gastroenterol Nutr.* 2011; 53(6):651–8. [PubMed: 21694637]
6. Katzka DA, et al. Accuracy, safety, and tolerability of tissue collection by Cytosponge vs endoscopy for evaluation of eosinophilic esophagitis. *Clin Gastroenterol Hepatol.* 2015; 13(1):77–83. [PubMed: 24997328]
7. Tabatabaei N, et al. Tethered confocal endomicroscopy capsule for diagnosis and monitoring of eosinophilic esophagitis. *Biomed Opt Express.* 2013; 5(1):197–207. [PubMed: 24466487]
8. Nicodeme F, et al. Esophageal distensibility as a measure of disease severity in patients with eosinophilic esophagitis. *Clin Gastroenterol Hepatol.* 2013; 11(9):1101–1107. [PubMed: 23591279]
9. Wen T, et al. Molecular diagnosis of eosinophilic esophagitis by gene expression profiling. *Gastroenterology.* 2013; 145(6):1289–99. [PubMed: 23978633]
10. Friedlander J, et al. Unsedated transnasal esophagoscopy for monitoring therapy in pediatric eosinophilic esophagitis. *Gastrointestinal Endoscopy.* In press.
11. Sami SS, et al. A randomized comparative effectiveness trial of novel endoscopic techniques and approaches for Barrett's esophagus screening in the community. *Am J Gastroenterol.* 2015; 110(1):148–58. [PubMed: 25488897]