



Published in final edited form as:

Gastrointest Endosc. 2016 February ; 83(2): 299–306.e1. doi:10.1016/j.gie.2015.05.044.

Unsedated transnasal esophagoscopy for monitoring therapy in pediatric eosinophilic esophagitis

Joel A. Friedlander, DO, MBe^{1,2}, Emily M. DeBoer, MD^{2,3}, Jason S. Soden, MD^{1,2}, Glenn T. Furuta, MD^{1,5}, Calies D. Menard-Katcher, MD^{1,5}, Dan Atkins, MD^{5,6}, David M. Fleischer, MD^{5,6}, Robert E. Kramer, MD¹, Robin R. Deterding, MD^{2,3}, Kelley E. Capocelli, MD⁷, and Jeremy D. Prager, MD^{2,4}

¹Digestive Health Institute, Children's Hospital Colorado, Section of Pediatric Gastroenterology, Hepatology, and Nutrition, University of Colorado School of Medicine, Aurora, Colorado, USA.

²Aerodigestive Program, Children's Hospital Colorado, Aurora, Colorado, USA.

³Breathing Institute, Children's Hospital Colorado, Section of Pulmonary Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA.

⁴Department of Otolaryngology, Children's Hospital Colorado, Department of Otolaryngology, University of Colorado School of Medicine, Aurora, Colorado, USA.

⁵Gastrointestinal Eosinophilic Diseases Program, Children's Hospital of Colorado, Aurora, Colorado, USA.

⁶Allergy Section, Children's Hospital Colorado, Section of Allergy, Immunology, and Rheumatology, University of Colorado School of Medicine, Aurora, Colorado, USA.

⁷Division of Pediatric Pathology, Children's Hospital of Colorado, Department of Pathology, University of Colorado School of Medicine, Aurora, Colorado, USA.

Abstract

Background and Aims—Unsedated transnasal endoscopy (TNE) is safer and less costly than sedated EGD. The aim of this study was to evaluate the performance of TNE with biopsies in monitoring the esophageal mucosa of pediatric patients with eosinophilic esophagitis.

Methods—Patients between 8 and 17 years of age with eosinophilic esophagitis and their parents were enrolled. Unsedated TNE was performed. A 2.8-mm (1.2-mm channel) or a 4-mm flexible bronchoscope (2-mm channel) was used, and esophageal biopsy specimens were obtained. Biopsy specimen analysis, duration, adverse events, and billing charges of TNE were assessed. Immediately after TNE and a minimum of 2 weeks later, a modified Group Health Association of America 9 survey and a preference questionnaire were completed, respectively.

Reprint requests: Joel A. Friedlander DO, MBe, Digestive Health Institute, Children's Hospital Colorado, Section of Pediatric Gastroenterology, Hepatology and Nutrition, University of Colorado School of Medicine, University of Colorado Anschutz Medical Campus, 13123 East 16th Avenue, B290, Aurora, CO 80045; If you would like to chat with an author of this article, you may contact Dr Friedlander at Joel.Friedlander@childrenscolorado.org.

DISCLOSURE: All other authors disclosed no financial relationships relevant to this article.

Results—Twenty-one of 22 enrolled patients underwent TNE. TNE was performed with no serious adverse events. Histopathological analysis revealed 0 eosinophils per high-power field ($n = 12$), fewer than 15 eosinophils per high-power field ($n = 4$), and more than 15 eosinophils per high-power field ($n = 5$). The total epithelial surface area of mucosal biopsy samples from either TNE Forceps (1.2 mm or 2 mm biopsy channel forceps) compared with those obtained during the subject's previous EGD by using standard endoscopic forceps was not statistically different ($P = .308$ [1.2 mm]/ $P = .492$ [2 mm]). All parents and 76.2% of subjects would undergo the TNE again. TNE was preferred over EGD by 85.7% of parents and 52.4% of subjects. The modified Group Health Association of America 9 survey revealed a high degree of satisfaction (average, 43.19 ± 2.6 ; maximum score, 45). Charges associated with TNE were 60.1% lower than for previous EGDs.

Conclusions—Unsedated TNE is an effective, lower-cost procedure for monitoring the esophageal mucosa of children with eosinophilic esophagitis.

Eosinophilic esophagitis (EoE) is an increasingly common chronic inflammatory disease that affects children and adults, with an estimated incidence of 1/10,000 in the United States.¹ Because of its potential to progress to esophageal stricture and the fact that symptoms do not always correlate with the degree of eosinophilia, much attention has been paid, including in the most recent 2014 guideline, to repeated assessment of the esophageal mucosa to ensure mucosal healing after treatment.^{2–5} In contrast, the risks, cost, and time commitment associated with traditional sedated EGD can be significant and have raised concerns for providers and parents alike.⁶ These dilemmas challenge the gastroenterologist to contemplate whether EGD use in EoE is meeting the triple aim in health care of Berwick et al⁷ to provide effective treatment, low-cost care, and an optimal and safe health care experience. Should EGD with biopsy be performed after each therapeutic change regardless of symptomatology, or should EGD be reserved for patients who are not clinically responding to treatment?

To address these questions, alternative methods are urgently needed to measure esophageal inflammation. Although esophagoscopy with biopsies remains the criterion standard technique for assessing mucosal inflammation, other technologies such as the Cytosponge (Medtronic, Minneapolis, Minn), esophageal string test, and confocal tethered endomicroscopy have emerged as potential alternatives.^{8–10} To date, these tools, although less invasive, are still available only in research settings.^{1,8}

Recent work has led to the development of transnasal endoscopy (TNE)/transnasal esophagoscopy) to assess the esophageal mucosa in adults.^{11–17} In contrast to traditional EGDs, TNE offers advantages including that it can be performed in an outpatient clinic room, requires no anesthesia or sedation, uses a small endoscope that is tolerated by adults, and obtains samples adequate for assessment of Barrett's esophagus.^{18,19} Although not studied to date in pediatric patients, experience using unsedated laryngoscopy in pediatric otolaryngology and pediatric pulmonology suggests that this technology could be adapted for sampling the mucosa of children with EoE.²⁰ We hypothesized that TNE was a safe and effective tool to monitor the mucosa of children with EoE. The aim of this study was to evaluate the performance of TNE with biopsies by using ultraslim flexible endoscopes to

assess the esophageal mucosa in pediatric subjects with EoE. This was done through the evaluation of parental and subject responses to TNE, the assessment of the ability to procure samples that would be adequate to monitor disease, monitoring adverse events, and recording procedure duration and the charges generated.

MATERIALS AND METHODS

Subjects 8 to 17 years of age between March 2014 and January 2015 with a diagnosis of EoE and who had undergone at least 1 previous EGD under anesthesia were recruited from the outpatient clinic at Children's Hospital Colorado. The diagnosis of EoE was made broadly according to published criteria that include symptoms referable to the esophagus, dense esophageal eosinophilia with more than 15 eosinophils per high-power field, and exclusion of other causes of mucosal eosinophilia that included either any trial of proton pump inhibitor or placement of a pH impedance probe before TNE.^{21,22} At the time of the scheduled clinically indicated follow-up appointment, subjects were approached if their primary GI provider thought that a follow-up esophagoscopy was needed to evaluate their clinical response to therapy. Subjects were queried as to whether they would be interested in having an unsedated TNE with movie distraction performed instead of a sedated EGD. If so, informed consent was obtained, and demographic data were collected.

Subjects were instructed to not eat or drink for 2 hours before the TNE. In a standard clinic room, subjects were asked to sit in a chair designed for outpatient laryngoscopic procedures. Two to 6 sprays of 4% aerosolized lidocaine were applied to the nares to achieve topical anesthesia. Subject distraction was accomplished by using either HMZ-T3W 3-dimensional movie goggles (Sony Corporation, Tokyo, Japan) or Cinemizer Goggles (Carl Zeiss AG, Oberkochen, Germany), depending on face size to facilitate viewing an immersive movie or television program of their choice. Parents remained in the room for the duration of the study. For study consistency and patient comfort, 1 of 2 experienced nasal laryngoscopy pulmonologists (E.D., R.D.) or 1 otolaryngologist (J.P.) performed transnasal laryngoscopy by using an Olympus BFXP160F 2.8-mm bronchoscope (1.2-mm biopsy channel/60-cm length) (Olympus America, Center Valley, Pa) in 11 of 21 subjects and 10 of 21 subjects by using a 4-mm BPMP160F (2-mm biopsy channel/60-cm length) ending with the endoscope in the proximal esophagus. The gastroenterologist (J.F.) performed esophagoscopy and biopsy sample collection (3 from the proximal and 3 from the distal esophagus). The stomach was visualized in limited view in all subjects. Visual confirmation of the adequacy of the biopsy specimens was performed before withdrawing the endoscope. Information on adverse events, subject symptoms, and duration of TNE (endoscope insertion to endoscope withdrawal) in 5-minute intervals up to 15 minutes were collected. After the procedure, families were asked to answer the modified Group Health Association of America 9 endoscopy satisfaction questionnaire and then were discharged home.

Subjects were called the evening of the procedure and more than 72 hours but not later than 14 days after the procedure to evaluate for any adverse events. A minimum of 2 weeks but not more than 10 weeks after TNE, the subjects and parents were asked to answer a nonvalidated, novel, electronic qualitative survey regarding their experience with TNE

(Supplement 1, available at www.giejournal.org). This was adapted from another instrument used in the Gastrointestinal Eosinophilic Diseases Program at Children's Hospital Colorado.

A single pediatric pathologist (K.C.), who was not blinded to the type of endoscopy performed, evaluated biopsy specimens to assess for adequacy, size of the sample, and inflammatory findings including the number of eosinophils. To ensure an adequate high-power field analysis, the total epithelial surface area used to count eosinophils was analyzed by using graphical software and analysis (cell-Sens Standard, Olympus America). This was accomplished by comparing the subject's available previous esophageal biopsy samples by using a standard 2.8-mm biopsy forceps with the 1.2- or 2-mm biopsy forceps specimens that were collected during TNE.

Charges from TNEs and subjects' previous isolated sedated EGD were collected to compare the cost of the 2 procedures. Subjects who underwent combined procedures that may have prolonged sedation such as pH probes, pH impedance probes, colonoscopy, or flexible sigmoidoscopy at their previous endoscopy were excluded from this calculation ($n = 12$). The University of Colorado Institutional Review Board (COMIRB-13-2721) approved all study procedures.

Statistical analysis

Data were recorded in a Red Cap Secure Database. Response data reported by subjects during the qualitative instrument was analyzed as average and mean \pm and standard deviation (SD). This was done to report subjects' responses as a group with variation. Surface area analysis to ensure adequate specimen size was performed by using a Student paired, nonparametric t test. This was performed to minimize variations that may occur due to unknown variation in subjects' esophageal mucosa. Charge analysis was performed by using a nonparametric, unpaired t test as a comparison of 2 similar population groups undergoing endoscopy with similar, but not identical, charges at each occurrence.

RESULTS

Of 22 subjects referred for endoscopy, 22 were contacted and 21 subjects (95.5%) enrolled in this study. The 1 female subject who declined chose not to participate because of "sensory issues." There were 13 male and 9 female subjects. Ethnicity of subjects included 19 white, 1 Native American, and 2 Hispanic. The average age \pm SD was 13.04 ± 2.7 years (range 8–17 years). Subjects 1 and 13 to 21 underwent TNE with the 4-mm endoscope and were 8 to 16 years of age. Subject numbers 2 to 12 underwent TNE with the 2.8-mm endoscope and were 10 to 17 years of age. The average \pm SD number of endoscopies previously performed on the subject cohort was 2.19 ± 1.12 . All subjects underwent TNE with no serious adverse events. The duration of TNE procedures decreased as the endoscopists (J.F., E.D., J.P., R.D.) became more experienced with TNE. Procedure times that were longer than 15 minutes were due to technical difficulties and the gastroenterologist's learning curve (Table 1). The youngest child was 8 years old and was able to tolerate the 4-mm endoscope without difficulty. Self-reported symptoms associated with the TNE included gagging and sore throat (Table 2). No adverse event was associated with any emergency department evaluation or unintended evaluation or treatment. One subject had a panic attack before the

procedure but was still able to complete the TNE without any additional medication. She had a history of an anxiety disorder. One subject had nasal irritation with a drop of blood noted; this was represented in the self-reported symptoms.

Postprocedure assessment revealed a high degree of satisfaction and comfort with the TNE immediately after (Table 3) and at subsequent survey (Supplement 1). A high percentage of subjects reported satisfaction with TNE, both child subjects (81%) and parents (90.5%). The majority of children (76.2%) would repeat TNE, and 100% of parental subjects were willing to have their child undergo the procedure again. More than half of the child subjects (52.4%) preferred TNE, with 4 subjects not preferring either TNE or sedated EGD, whereas 85.7% of parental subjects preferred TNE for their child. Reasons for parental preference of TNE included no anesthesia (61.9%), faster procedure and recovery (52.3%), parental presence during the procedure (28.5%), and lower cost (19%).

Visual TNE findings are presented in Table 4. Visual findings correlated with the appropriate histologic findings in 85.7% of subjects. In those subjects in whom visual and histological findings did not correlate, 2 subjects with visual furrowing had normal biopsy findings, and 1 with normal-appearing mucosa showed histologic evidence of eosinophilia (<15 eosinophils per high-power field) (Fig. 1, Table 4)

Biopsy specimen adequacy evaluation and results are noted in Table 4. No significant difference was identified when comparing total epithelial surface area of the matched subjects' previous EGD by using either 1.2- or 2-mm forceps. Although there appears to be a surface area difference between the two 2.8-mm forceps control groups, subanalysis revealed no significant difference ($P = .136$). Global size differences of the biopsy samples were noted due to the presence or the absence of lamina propria. In this study, 1.2-mm forceps grasping 3 samples obtained $0.4 \times 0.2 \times 0.1$ -cm aggregate tissue, whereas 2-mm forceps obtained $0.4 \times 0.2 \times 0.2$ cm in total. EGD grasping 2 samples by using 2.8-mm forceps obtained $0.3 \times 0.3 \times 0.2$ -cm in aggregate sample.

Of the 21 subjects who underwent TNE, 11 had charge data that included an isolated EGD without additional charges for extended procedures and was available for analysis. Charges for each TNE subject, on average, were calculated to be $60.1 \pm 10.7\%$ less than their previous sedated EGD with biopsies, including anesthesia, pathology, facility fees, and physician fees. The average combined total charge of 11 sedated EGDs was $\$9390.79 \pm \2224.42 compared with $\$3547.96 \pm \254.42 for TNE. This represented a reduction of 62.2% in the total billed charges.

DISCUSSION

The emergence of EoE has led to a renewed interest in determining pathogenic mechanisms of esophageal inflammation and sampling of the esophageal mucosa to assess for mucosal healing. Despite the rapid progress in establishing diagnostic criteria, treatments, and novel genes related to pathogenic mechanisms that can significantly affect EoE patients, limited data are available to document the natural history of EoE. This lack of understanding has led to the current clinical practice of multiple, high-cost, and sedated assessments of the

esophageal mucosa to ascertain whether eosinophilia has resolved after treatment. If eosinophilia resolves, a predicate determination is made that the likelihood for EoE-related adverse events is diminished.²³ If eosinophilia persists, efforts are made to resolve inflammation with its subsequent impact on quality of life and costs of care. In this regard, novel devices and sampling methodologies are urgently needed. To address this and offer a new tool in the evaluation of EoE, we sought to determine whether TNE could sample the esophageal mucosa in a way that was well tolerated and adequate. In light of the emergent need for more efficient methods of esophageal mucosal evaluation in EoE, we performed this study within the confines of a multidisciplinary team to perform TNE with biopsies in a pediatric population. We chose this population because of the urgent need to minimize the repetitive risks of anesthesia, to improve the understanding of EoE pathogenesis, and to ultimately identify novel therapeutic targets.

Unsedated TNE is an established technique in a number of pediatric and adult subspecialties, but it has not been used commonly by pediatric gastroenterologists.^{11–17} A number of studies have described the advantages, limitations, and challenges of TNE use, and in 2010, the American Society for Gastrointestinal Endoscopy developed a guideline for the use of TNE in adults.^{24–27} This guideline increased attention to cost containment, and the recent upswing in interest in esophageal diseases led to renewed interest in this technique.^{25,28–30} A recent study also demonstrated the utility of TNE in adults with Barrett's esophagus.^{27,28,31} To date, only 1 study evaluated unsedated transoral endoscopy in children and concluded that it improved time and safety in assessing 21 children for evaluation of abdominal pain, dyspepsia, and dysphagia.³²

With the rapidly increasing prevalence of EoE, limited knowledge regarding its pathophysiology, and emerging clinical needs to assess the esophageal mucosa, we sought to determine whether TNE in pediatric EoE would be a feasible and efficacious tool. Results of our study reveal that patients and parents experienced with sedated EGD tolerate TNE well and that patients and their parents prefer TNE compared with EGD. It is likely that the limited side-effect profile and complete lack of serious adverse events contributed to the finding that 52.4% of pediatric subjects (4 subjects preferring neither EGD nor TNE) and 85.7% of parents (1 parent preferring neither TNE nor EGD) preferred unsedated TNE to sedated EGD. In that parents often make decisions about procedures in pediatrics and a majority of children prefer TNE, these percentages are suggestive of a successful alternative to EGD. Immediate benefits of this preference for patients include improved patient satisfaction and increased safety by eliminating anesthesia.

In many ways, our results are quite similar to those reported in adult studies. For example, a large Canadian study by Cho et al³⁰ evaluating 231 patients with an average age of 57 years for routine TNE found that TNE was well tolerated, safe, and feasible. This study was different, however, in that the patients were primarily adults, the endoscope used was larger (5.3 mm), and duodenal intubation was performed. Our study evaluated the use of 2 smaller endoscopes, smaller biopsy forceps, and TNE performance in children. The difference between our findings and those of similar adult studies is that in our study, both the parents and child subjects evaluated the technique, the adequacy of smaller forceps to evaluate the esophageal mucosa in EoE was assessed, and the actual rather than contemplative type of

future endoscopy preferred by subjects who have undergone multiple previous EGDs was examined. These findings strengthen the results of this research and its potential application to adult and pediatric endoscopy practices.

We are particularly encouraged by our findings for several reasons. First, there was great interest in this procedure among patients and parents. We only needed to screen 22 subjects to enroll the 21 subjects reported here. Both parents and children expressed a high level of satisfaction and enthusiasm to repeat unsedated TNE rather than standard EGD. Factors contributing to these responses included the lack of anesthesia, the presence of parents during the procedure, the limited duration of the procedure and rapid recovery, and improvement in their quality of life with TNE. They noted that it allowed them the ability to return to school, sports, eating, and work shortly afterward. The total time required for a standard EGD is 3 hours compared to 60 to 90 minutes required for the TNE. The 60- to 90-minute time for TNE in clinic included research documentation (30–45 minutes), preprocedural documentation/staff arrival/equipment setup (5–20 minutes), the procedure of TNE (5–15 minutes), and discharge instructions/questions (5–10 minutes). This 3-hour procedure center time for EGD usually includes check in; preoperative evaluation by nursing, gastroenterology, and anesthesia; the procedure itself; recovery; and discharge instructions. Most of these improvements in time reduction and increased satisfaction, noted above, are related to the effects of eliminating anesthesia or sedation for TNE. Not only does this practice seem to improve the satisfaction of patients and parents, but there is also a significant likelihood that it decreases the risk of adverse medication reactions, aspiration, and possible effects on the developing pediatric brain.⁶ TNE was also demonstrated to be safe, as evidenced by the fact that no serious adverse events or other event needed subsequent treatment or evaluation. This is an emerging concern among pediatric anesthesiologists.⁶

The second positive outcome of our study relates to the integrity of the mucosal sample. Regarding the technique's effectiveness in evaluating mucosal esophageal samples, we found that the epithelial surface area needed for eosinophil count evaluation was not significantly different from that of the standard EGD 2.8-mm biopsy forceps compared with either of the TNE 2-mm or 1.2-mm biopsy forceps, regardless of number of biopsy samples obtained. This finding provides a high level of confidence that the sample obtained at the time of TNE will have the same surface area compared with that obtained with the criterion standard EGD biopsy forceps. The 2-mm forceps were also able to procure lamina propria.

The final areas of interest in this study were the reduction in cost and increase in efficiency. Financial benefits of TNE include the fact that TNE incurred fewer charges and required less time away from school and work compared with a standard sedated pediatric EGD. The project demonstrated a significant decrease in patient charges. The majority of this reduction in cost is related to the lack of anesthesia/anesthesiologist during TNE. The significance of this cannot be understated. For example, if our institution were to perform 100 sedated EGDs per year for EoE at a noninsurance adjusted charge of \$9391 per general anesthesia-provided endoscopy encounter, this would accumulate \$939,100 in total charges per year for EoE. This would include all facility charges, physician, pathology, and anesthesia fees. If

these 100 EGDs for EoE were converted to unsedated TNE (\$3548), this could translate to a health care systems charge savings of \$584,300 per year.

Several areas require more investigation. First, for practical reasons, we needed to use 2 different sizes of endoscopes for TNE and did not evaluate gastric or duodenal tissue. Future studies will standardize this for patient comfort, a more complete evaluation, and biopsy sample size. For example, the endoscopist in this study found that the short 4-mm endoscope was easier to manipulate, allowed for obtaining double or triple biopsy samples in a single forceps pass, and generated faster endoscopy times. Technical optimization of the TNE for a larger esophageal lumen or evaluation of gastric or duodenal tissues could be performed. Second, although the 1.2-mm forceps were not able to procure lamina propria, the 2-mm forceps in this study were able to obtain lamina propria. Although this section of the tissue has been used to grade fibrosis, this metric has not been standardized or become a criterion standard for clinical assessments. Further, another method of variation that may have affected surface area analysis includes variability in sample procurement technique, a non-blinded clinical pathologist, and differences in quality of tissue samples depending on disease severity. Our study represents an initial assessment to test feasibility in pediatrics, but evaluating a much larger cohort is required to achieve a significant power for safety, prevent significant selection bias, and obtain other metrics. Power analysis based on our own institution's quality and safety data would necessitate more than 10,000 endoscopies to find a single significant adverse event. This could be remedied by the development of further databases because this technique is increasingly used at our institution or in a national program evaluating its use in pediatrics. Finally, we undertook this study in a multidisciplinary collaboration with our pediatric pulmonary and otolaryngology colleagues. This was done for study design to maximize patient comfort during TNE development in pediatrics; to kindle a strong interest in aerodigestive and eosinophilic disorders by gastroenterologists, otolaryngologists, and pulmonologists alike; and the need for a more pragmatic multidisciplinary approach to diagnosing and managing EoE as it presents in different single-specialty clinics. Additional areas of study weakness are recall bias regarding experiences with previous EGDs that may have affected the qualitative instrument and selection bias of children undergoing follow-up endoscopy of a recently diagnosed condition in a nonrandomized small sample. A larger sample size for further study may clarify these points. We are confident, however, that this is a technically feasible procedure and are further encouraged by its overall rapid success that was facilitated by a multidisciplinary pediatric team dedicated to the care of children with aerodigestive diseases and EoE.

In conclusion, the implementation of TNE in pediatric gastroenterology for the evaluation of pediatric EoE is safe, is preferred by patients and parents alike, and has the potential to dramatically reduce costs. Thus, it appears that TNE would be measured as an effective practice in pediatric EoE management per the description by Berwick et al⁷ of the triple aim: the pursuit of improved experience of care, the health of populations should be improved, and the cost of per capita health care should be decreased. This suggests that TNE use should be considered as an alternative to standard sedated EGD or esophagoscopy for the follow-up evaluation of pediatric EoE. Our study provides strong support for larger studies to validate this approach that will provide novel insights into the natural history of EoE and

significantly improve the lives of children with EoE in a safer, cost-effective, and efficacious manner. The technique will continue to be refined and improved, offering more opportunities for its use in monitoring response to therapeutics, obtaining follow-up evaluations, and performing research in EoE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Dr Friedlander is a consultant for QOL Medical LLC. Dr Furuta is supported by NIH grant 1K24DK100303. NIH/NICRR Colorado CTSI grant number UL1 TR001082 (Red Cap). Dr DeBoer is supported by NIH/NCATS Colorado CTSI grant KL2 TR001080. Dr Prager is supported by Surgery Research Partnership grant PGO100481.

Abbreviations

EoE	eosinophilic esophagitis
SD	standard deviation
TNE	transnasal endoscopy

References

1. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Am J Gastroenterol*. 2013; 108:679–92. quiz 693. [PubMed: 23567357]
2. Stucke EM, Clarridge KE, Collins MH, et al. The value of an additional review for eosinophil quantification in esophageal biopsies. *J Pediatr Gastroenterol Nutr Epub*. 2015 Jan 28.
3. Kagalwalla AF, Sentongo TA, Ritz S, et al. Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2006; 4:1097–102. [PubMed: 16860614]
4. Greenhawt M, Aceves SS, Spergel JM, et al. The management of eosinophilic esophagitis. *J Allergy Clin Immunol Pract*. 2013; 1:332–40. quiz 341–2. [PubMed: 24565538]
5. Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. *J Pediatr Gastroenterol Nutr*. 2014; 58:107–18. [PubMed: 24378521]
6. Gleich SJ, Flick R, Hu D, et al. Neurodevelopment of children exposed to anesthesia: design of the Mayo Anesthesia Safety in Kids (MASK) study. *Contemp Clin Trials*. 2014; 41C:45–54. [PubMed: 25555440]
7. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood)*. 2008; 27:759–69. [PubMed: 18474969]
8. Furuta GT, Kagalwalla AF, Lee JJ, et al. The oesophageal string test: a novel, minimally invasive method measures mucosal inflammation in eosinophilic oesophagitis. *Gut*. 2013; 62:1395–405. [PubMed: 22895393]
9. Tabatabaei N, Kang D, Wu T, et al. Tethered confocal endomicroscopy capsule for diagnosis and monitoring of eosinophilic esophagitis. *Biomed Opt Express*. 2013; 5:197–207. [PubMed: 24466487]
10. Katzka DA, Geno DM, Ravi A, et al. Accuracy, safety, and tolerability of tissue collection by Cytosponge vs endoscopy for evaluation of eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2015; 13:77–83.e2. [PubMed: 24997328]

11. Birkner B, Fritz N, Schatke W, et al. A prospective randomized comparison of unsedated ultrathin versus standard esophagogastroduodenoscopy in routine outpatient gastroenterology practice: does it work better through the nose? *Endoscopy*. 2003; 35:647–51. [PubMed: 12929058]
12. Dumortier J, Josso C, Roman S, et al. Prospective evaluation of a new ultrathin one-plane bending videoendoscope for transnasal EGD: a comparative study on performance and tolerance. *Gastrointest Endosc*. 2007; 66:13–9. [PubMed: 17591468]
13. Dumortier J, Ponchon T, Scoazec JY, et al. Prospective evaluation of transnasal esophagogastroduodenoscopy: feasibility and study on performance and tolerance. *Gastrointest Endosc*. 1999; 49:285–91. [PubMed: 10049409]
14. Hu CT. Gauze pledgetting versus endoscopic-guided aerosolized spray for nasal anesthesia before transnasal EGD: a prospective, randomized study. *Gastrointest Endosc*. 2010; 71:11–20. [PubMed: 19748613]
15. Mokhashi MS, Wildi SM, Glenn TF, et al. A prospective, blinded study of diagnostic esophagoscopy with a superthin, stand-alone, battery-powered esophagoscope. *Am J Gastroenterol*. 2003; 98:2383–9. [PubMed: 14638337]
16. Mulcahy HE, Riches A, Kiely M, et al. A prospective controlled trial of an ultrathin versus a conventional endoscope in unsedated upper gastrointestinal endoscopy. *Endoscopy*. 2001; 33:311–6. [PubMed: 11315891]
17. Yagi J, Adachi K, Arima N, et al. A prospective randomized comparative study on the safety and tolerability of transnasal esophagogastroduodenoscopy. *Endoscopy*. 2005; 37:1226–31. [PubMed: 16329022]
18. Shariff MK, Bird-Lieberman EL, O'Donovan M, et al. Randomized crossover study comparing efficacy of transnasal endoscopy with that of standard endoscopy to detect Barrett's esophagus. *Gastrointest Endosc*. 2012; 75:954–61. [PubMed: 22421496]
19. Saeian K, Staff DM, Vasilopoulos S, et al. Unsedated transnasal endoscopy accurately detects Barrett's metaplasia and dysplasia. *Gastrointest Endosc*. 2002; 56:472–8. [PubMed: 12297760]
20. Wood RE. Evaluation of the upper airway in children. *Curr Opin Pediatr*. 2008; 20:266–71. [PubMed: 18475094]
21. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology*. 2007; 133:1342–63. [PubMed: 17919504]
22. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol*. 2011; 128:3–20 e6. quiz 21–2. [PubMed: 21477849]
23. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. *Gastroenterology*. 2013; 145:1230–6. e1–2. [PubMed: 23954315]
24. ASGE Technology Committee. Rodriguez SA, Banerjee S, Desilets D, et al. Ultrathin endoscopes. *Gastrointest Endosc*. 2010; 71:893–8. [PubMed: 20438882]
25. Faulx AL, Catanzaro A, Zyzanski S, et al. Patient tolerance and acceptance of unsedated ultrathin esophagoscopy. *Gastrointest Endosc*. 2002; 55:620–3. [PubMed: 11979240]
26. Faulx AL, Vela S, Das A, et al. The changing landscape of practice patterns regarding unsedated endoscopy and propofol use: a national Web survey. *Gastrointest Endosc*. 2005; 62:9–15. [PubMed: 15990813]
27. Tatsumi Y, Harada A, Matsumoto T, et al. Current status and evaluation of transnasal esophagogastroduodenoscopy. *Dig Endosc*. 2009; 21:141–6. [PubMed: 19691759]
28. Chak A, Alashkar BM, Isenberg GA, et al. Comparative acceptability of transnasal esophagoscopy and esophageal capsule esophagoscopy: a randomized, controlled trial in veterans. *Gastrointest Endosc*. 2014; 80:774–82. [PubMed: 24973176]
29. Lin LF, Shen HC. Unsedated transnasal percutaneous endoscopic gastrostomy carried out by a single physician. *Dig Endosc*. 2013; 25:130–5. [PubMed: 23362930]
30. Cho S, Arya N, Swan K, et al. Unsedated transnasal endoscopy: a Canadian experience in daily practice. *Can J Gastroenterol*. 2008; 22:243–6. [PubMed: 18354752]

31. Bush CM, Postma GN. Transnasal esophagoscopy. *Otolaryngol Clin North Am.* 2013; 46:41–52. [PubMed: 23177404]
32. Bishop PR, Nowicki MJ, May WL, et al. Unsedated upper endoscopy in children. *Gastrointest Endosc.* 2002; 55:624–30. [PubMed: 11979241]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

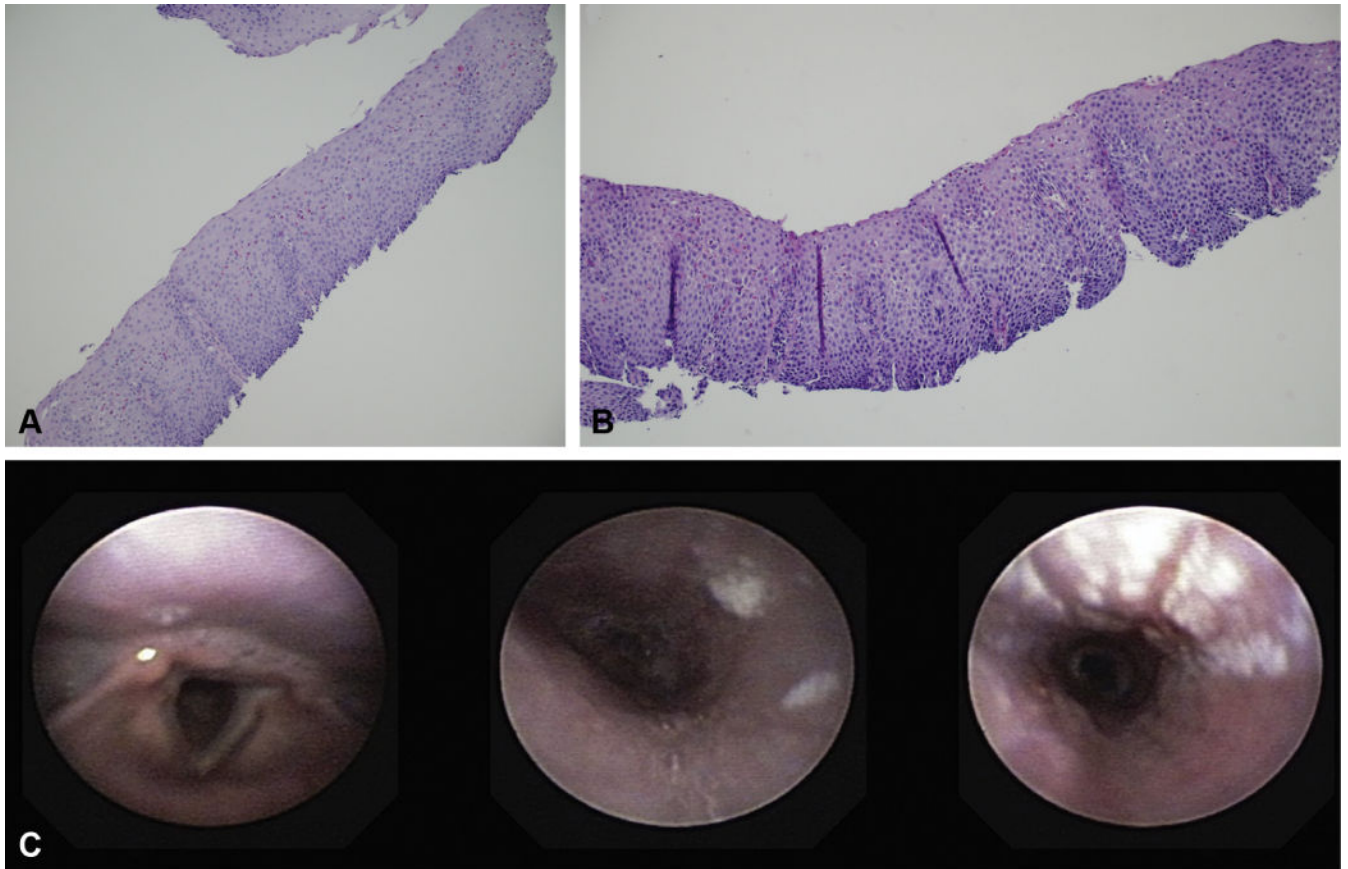


Figure 1.

Visual and microscopic findings of eosinophilic esophagitis (EoE) by using transnasal endoscopy (TNE). **A**, Biopsy sample with active EoE by using standard 2.8-mm EGD forceps: surface area, 0.10 mm². **B**, Biopsy sample from the same patient with active EoE by using TNE 1.2-mm forceps: surface area, 0.12 mm². **C**, Subject with active furrowing and eosinophilic exudates.

TABLE 1

Duration of TNE*

Duration of TNE, min	No. of subjects	TNE subject number
5–10	10	10, 13, 14, 15, 16, 17, 18, 19, 20, 21
10–15	8	2, 3, 4, 5, 8, 9, 11, 12
>15	3	1, 6, 7

TNE, Transnasal endoscopy.*
Time from the insertion to removal of the endoscope.

TABLE 2

Adverse events

Self-reported symptom from instrument	Total subjects
Nausea	4
Choking/gagging	12
Sore throat	10
Vomiting	2
Chest pain	2
Abdominal pain	1
Other	4 (2 nose discomfort, 2 slight sore throat)
No significant symptoms	7

TABLE 3

Satisfaction with procedure

Instrument/question	Instrument score
mGHAA-9 score \pm SD (maximum of 45 points)	43.19 \pm 2.6
Qualitative satisfaction instrument, 21 subjects, no. (%)	
Child: satisfaction with TNE	17 (81)
Parent: satisfaction with TNE	19 (90.5)
Parent/child concerned about TNE	8 (28.6)
Parent/child satisfied with sedated EGD	17 (81)
Parent/child concerned about sedated EGD	13 (61.9)
Child: willing to repeat TNE	16 (76.2)
Parent: willing to repeat TNE	21 (100)
Child: prefer to repeat TNE	11 (52.4), 4 preferred neither EGD nor TNE
Parent: prefer to repeat TNE	18 (85.7), 1 preferred neither EGD nor TNE
Parent: qualitative advantages of TNE	13/21, no anesthesia; 11/21, faster procedure and recovery; 6/21, parental presence in procedure room; 4/21, lower cost

mGHAA-9, Modified Global Hospital Association 9; *SD*, standard deviation; *TNE*, transnasal endoscopy.

TABLE 4

TNE findings

TNE findings	Total no. of specimens
Visually normal	11
Slight furrowing	2
Furrowing	8 (1 with exudates)
Normal biopsy	12
Eosinophils >15 hpf	5
Eosinophils <15 hpf	4

Biopsy forceps	Sample size	Average \pm SD epithelial surface area, mm ²	P value
EGD: 2.8-mm* biopsy forceps	n = 11	0.38 \pm 0.14	.308
TNE: 1.2-mm biopsy forceps		0.33 \pm 0.09	
EGD: 2.8-mm* biopsy forceps	n = 10	0.51 \pm 0.18	.492
TNE: 2.0-mm biopsy forceps		0.50 \pm 0.14	

TNE, Transnasal endoscopy; *hpf*, high-power field; *SD*, standard deviation.

* *P* value of .136 comparing both 2.8-mm groups.