



American Society for Gastrointestinal Endoscopy consensus recommendations on the endoscopic management of eosinophilic esophagitis—part 2: disease assessment, monitoring, and pediatric considerations CME

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Esophagogastroduodenoscopy is essential to evaluate symptoms of suspected eosinophilic esophagitis (EoE), assess endoscopic findings, obtain biopsy specimens for histopathologic evaluation, perform esophageal dilation, confirm the diagnosis, and monitor the condition. The American Society for Gastrointestinal Endoscopy (ASGE) previously provided consensus recommendations on the approach to endoscopy in EoE across topics of endoscopic diagnosis, endoscopic grading, and esophageal dilation. Because additional areas of endoscopy still required guidance, we performed an independent modified Delphi process focusing on pediatric considerations, disease assessment, and disease monitoring. A core group of EoE experts reviewed published guidelines and developed a set of patient-centered recommendation statements informed by literature review. A multidisciplinary group of adult and pediatric international EoE experts then voted on the statements over 2 Delphi rounds. All statements with 80% agreement were accepted for inclusion. This process yielded 28 consensus statements. Pediatric-specific statements covered when to suspect EoE and perform endoscopy, how to grade endoscopic severity, and when and how to perform esophageal dilation in children. Statements across all age ranges addressed the role of less-invasive monitoring, performing diagnostic endoscopy off treatment, the need to consider symptoms, endoscopic features, and histologic findings when assessing disease activity, treatment-based monitoring intervals, and the approach to esophageal biopsies during monitoring. Coupled with the original consensus work, we provide a comprehensive endoscopic approach to EoE as well as practical guidance for procedure-related aspects in the field to facilitate high-quality endoscopic care to patients with EoE. (Gastrointest Endosc 2026;103:396-417.)

(footnotes appear on last page of article)

INTRODUCTION

Esophagogastroduodenoscopy (EGD) is essential for diagnosis and management of eosinophilic esophagitis (EoE).¹ This chronic, allergen/immune-mediated disease is characterized by a progression from inflammation to fi-

brostenosis, with associated symptoms of esophageal dysfunction and adverse events of stricture formation and esophageal food impaction.²⁻⁴ EGD is performed to evaluate symptoms of suspected EoE, assess endoscopic findings of EoE, obtain biopsy specimens for histopathologic evaluation, and perform esophageal dilation.^{5,6} After

initial evaluation and throughout the disease course, endoscopy is performed to assess response to treatment and monitor disease activity.⁷

Given the central role of endoscopy in EoE, the American Society for Gastrointestinal Endoscopy (ASGE) previously convened a multidisciplinary consensus conference to provide recommendations on use of endoscopy in EoE.¹ That original Delphi process yielded 20 recommendations that reached consensus across topics of endoscopic diagnosis, endoscopic grading, and esophageal dilation, with 1 statement on disease monitoring; 8 additional statements were not accepted. Key among the accepted statements were recommendations for taking esophageal biopsy specimens (location, number, timing, including during procedures to remove impacted food boluses), classifying endoscopic findings using the EoE Endoscopic Reference Score (EREFS), and using a “start low and go slow” approach to esophageal dilation.

Although those guideline statements were comprehensive, several topics related to endoscopy in EoE were not covered, and a second ASGE consensus conference was merited to address these gaps considering rapid advancements in our understanding of the disease state and the evolving knowledge base in the field. The overriding goal remained to provide recommendations for best practices related to endoscopy while expanding the focus to topics that were either not covered in detail or not addressed during the prior ASGE consensus process including pediatric considerations, disease assessment, and disease monitoring. We were cognizant of not repeating what was accomplished with the prior ASGE work,¹ and not duplicating other recent guidelines on EoE diagnosis, treatment, and monitoring.^{4,7}

METHODS

We performed a Delphi process using a modified version of the RAND/University of California Los Angeles Appropriateness Methodology, as previously described (Fig. 1).⁸⁻¹¹ In brief, a core group of 6 EoE experts (E.D., G.F., D.K., J.L., A.M., P.S.) were selected by ASGE leadership to guide the exercise, and this group reviewed published guidelines and literature to develop a set of patient-centered statements focusing on the areas of interest identified: pediatric considerations, disease assessment, and disease monitoring. Meetings were held with the core group on a virtual video platform, and the patient-centered statements were accepted. Next, a search librarian assisted in performing a systematic review through PubMed, Cochrane Library, and Embase for each of the questions; the core group also identified pertinent articles for inclusion. Literature search parameters included a search date of January 1, 1993, to September 21, 2024, in English language only and excluding animal studies, review studies, and conference articles. The

year 1993 was chosen as the start date because that is when the first report of EoE was published. The results of this literature review were used to inform and support a set of 28 initial recommendation statements, which were again reviewed and accepted by the core group.

A multidisciplinary group of 21 additional adult and pediatric international EoE experts was then identified based on research and publication record, invitations for speaking at national or international conferences, participation in clinical trials, and extensive clinical expertise. The 28 statements were circulated to this wider expert group using an online voting platform. Experts were asked to rank the statement on an acceptability scale of 1 (completely disagree) to 9 (completely agree), and a statement was accepted if at least 80% of participants scored the statement from 7 to 9, similar to the prior methodology used.¹ After the first round of Delphi voting, 27 of 28 statements achieved the acceptability threshold. We then convened a virtual meeting using a video platform to discuss the statement that was not accepted, the statement was rewritten, an opportunity for other statements to be discussed was provided, a second round of online voting was conducted, and the revised statement was accepted. The list of statements is presented in Table 1, and the evidence and rationale behind the statements follows.

RESULTS

Pediatric considerations

1. In children 18 months and younger, endoscopy for suspected EoE should be performed when there are chronic feeding difficulties, failure to advance diet in terms of varied textures, or malnutrition or poor weight gain.

Diagnosis of EoE in very young children requires a high level of clinical suspicion, as infants and toddlers are developmentally incapable of self-reporting symptoms.^{12,13} Parents may report their child has difficulties with advancing solid foods, delayed oral feeding skills, low volume of intake, and prolonged mealtimes.¹³⁻¹⁵ Chronic poor nutrition from maladaptive feeding behaviors may affect weight gain and other growth parameters. As such, it is important to consider performing endoscopy in very young children with chronic feeding difficulties, failure to advance to varied food textures, malnutrition, or poor weight gain.^{13,15,16} These symptoms can indicate esophageal inflammation and dysfunction, as well as many other non-EoE conditions,¹⁷ in patients who are too young to verbalize symptoms of dysphagia or pain.¹⁸ Endoscopy allows for direct visualization of the esophagus and biopsy sampling to confirm or exclude a diagnosis of EoE.¹⁸⁻²² Early diagnosis and treatment are essential to prevent longer-term adverse events, such as feeding aversion,^{13,15} growth failure,^{16,23} and esophageal remodeling and strictures.^{24,25}

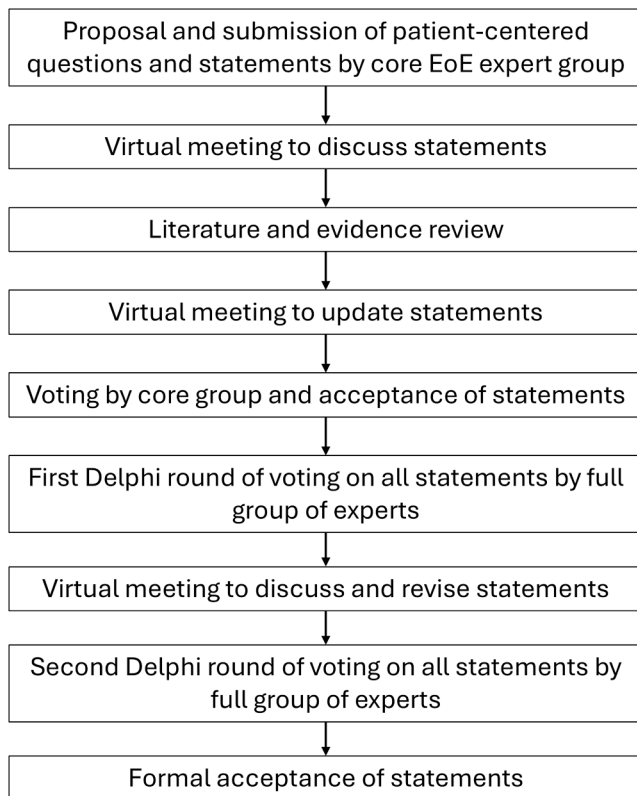


Figure 1. Overview of Delphi and consensus process. *EoE*, eosinophilic esophagitis.

2. In children older than 18 months, endoscopy for suspected EoE should be considered for protracted vomiting or reflux symptoms, abdominal pain, failure of feeding therapies, dysphagia, or food impaction.

Although dysphagia is the most common self-reported symptom of EoE in adults, it is a less common symptom in children who can verbalize.²⁶⁻²⁸ Adaptive symptoms can be present to avoid the discomfort with dysphagia. In addition, children and adolescents often present with a broader range of symptoms that can include but are not limited to protracted vomiting, treatment-refractory reflux, chronic abdominal pain, failure of feeding therapies, and food impaction. Recent studies have attested to the deleterious impact of these chronic symptoms on quality of life.^{29,30} Symptoms that suggest esophageal dysfunction necessitate endoscopy with biopsy, which is critical to identify pediatric EoE^{17,22,23} and may also be necessary to investigate other underlying etiologies.^{19,31} For example, a retrospective study of biopsies from children in 14 European and Middle Eastern countries suggests that up to 7.6% of children undergoing endoscopy for diagnosis of EoE may also have *Helicobacter pylori*.³¹ Regardless of comorbidities, early diagnosis of EoE has been shown to allow for timely intervention to prevent disease progression,²⁷ feeding difficulties,^{15,32} and long-term adverse events like strictures and/or esophageal

dysfunction.^{24,25} For example, in 2 retrospective cohort studies, odds of stricture development was about three-quarters lower for patients with early treatment and histologic response than those who did not respond to treatment.^{24,25}

3. In children of any age, endoscopy should be performed when there is a high index of suspicion for EoE based on a patient's symptoms, concomitant atopic conditions, or family history of atopy or EoE.

Patient medical history of atopic conditions (such as asthma, allergic rhinitis, eczema, or food allergies), and family history of atopy significantly increase the likelihood of diagnosing EoE, which is strongly associated with allergic conditions and can help predict EoE clinically.³³ Approximately 80% of patients with EoE have comorbid atopic disorders, including IgE-mediated food allergy, seasonal allergies, atopic dermatitis, and asthma.^{34,35} Further, EoE is also more commonly found in patients with atopic disease compared with those without atopy,³⁶⁻⁴⁰ and it is suggested that EoE is a late manifestation of the allergic march.⁴⁰ Therefore, EoE should be considered when children with atopia have GI symptoms consistent with esophageal dysfunction. Family history of all atopic conditions, including EoE itself, also elevates risk of EoE⁴¹⁻⁴⁴ and helps increase the clinical suspicion of EoE. As discussed above, endoscopy with biopsies is essential to confirm the diagnosis, as the symptoms of EoE can overlap with other conditions, including non-IgE- and IgE-mediated allergic disorders and GI diseases.⁴⁵

4. In children with suspected EoE, esophageal, gastric, and duodenal biopsy specimens should be obtained. Specifically, there should be at least 6 biopsy specimens total taken from at least 2 levels in the esophagus. The number of gastric and duodenal biopsy specimens should be sufficient for evaluation of suspected clinical conditions of interest.

In all children with suspected EoE, obtaining esophageal, gastric, and duodenal biopsy specimens is critical for diagnosis and exclusion of other conditions.^{2,4,20} Best practices in tissue acquisition, as supported by evidence from both pediatric and adult studies, emphasize obtaining at least 6 esophageal biopsy specimens from at least 2 levels of the esophagus, for example in the proximal and distal esophagus, as mucosal eosinophil distribution can vary significantly within the esophagus.⁴⁶⁻⁵² Taking fewer biopsy specimens may miss areas of diagnostic significance, although the sensitivity for detecting ≥ 15 eosinophils/HPF improves substantially with multiple biopsy specimens, particularly from areas that are endoscopically abnormal.⁴⁹ Although 6 esophageal biopsy specimens optimize diagnostic yield for EoE, the number of gastric and duodenal biopsies should be sufficient to evaluate suspected clinical conditions of interest, including non-EoE eosinophilic gastrointestinal diseases (EGIDs), celiac disease, *H pylori* and other infections, autoimmune enteropathy, and others.⁴ In general, the yield of gastric and

TABLE 1. Consensus statements and percent agreement reached for the endoscopic approach to EoE

Statement	Percent agreement*
Pediatric considerations	
1. In children 18 months and younger, endoscopy for suspected EoE should be performed when there are chronic feeding difficulties, failure to advance diet in terms of varied textures, or malnutrition or poor weight gain.	92
2. In children older than 18 months, endoscopy for suspected EoE should be considered for protracted vomiting or reflux symptoms, abdominal pain, failure of feeding therapies, dysphagia, or food impaction.	96
3. In children of any age, endoscopy should be performed when there is a high index of suspicion for EoE based on a patient's symptoms, concomitant atopic conditions, or family history of atopy or EoE.	96
4. In children with suspected EoE, esophageal, gastric and duodenal biopsy specimens should be obtained. Specifically, there should be at least 6 biopsy specimens total taken from at least 2 levels in the esophagus. The number of gastric and duodenal biopsy specimens should be sufficient for evaluation of suspected clinical conditions of interest.	92
5. In children with known EoE, biopsy specimens obtained during monitoring endoscopies can be limited to the esophagus if prior gastric and duodenal biopsy specimens were normal, the stomach and duodenum appear normal, and there are no new symptoms to suggest gastric or small intestinal pathology.	92
6. Providers should document the EoE Endoscopic References Score (EREFS) in all children undergoing endoscopic procedures with suspected or known EoE to allow for initial and longitudinal assessment of endoscopic severity.	100
7. In children with EoE, esophageal string testing and unsedated transnasal endoscopy (uTNE) should be reserved for monitoring disease status. Providers should not use either modality to establish an EoE diagnosis.	84
8. In children with EoE, esophageal dilation should be considered in patients with symptomatic strictures or narrow-caliber esophagus on esophagram or endoscopy regardless of disease activity.	88
9. Fluoroscopic imaging of the esophagus may be appropriate for evaluating children with dysphagia but should be recognized to have limited sensitivity and specificity for identifying strictures or determining esophageal caliber.	84
10. Providers should consider initiating feeding therapy in children with EoE who have chronic feeding difficulties, taking into consideration inflammatory and fibrostenotic disease activity, specific dietary needs, and goals of feeding therapy.	96
11. Providers should carefully assess readiness and address preprocedure anxiety levels in older adolescents and young adults before performing either sedated or unsedated endoscopic procedures.	88
12. Providers should implement a structured transition plan from pediatric to adult care in patients with EoE.	100
Disease assessment	
13. In a patient with suspected EoE, the initial EGD should be performed off treatment.	84
14. In a patient with suspected EoE, a standard EGD should initially be performed to allow for comprehensive assessment (including gastric and duodenal biopsy specimens when indicated) and esophageal dilation of a symptomatic stricture if needed.	92
15. All patients who have symptoms or endoscopic findings consistent with EoE should have esophageal biopsy specimens obtained.	100
16. The definitive role of functional luminal imaging planimetry in the routine care of patients with EoE has yet to be determined.	84
17. When assessing disease activity in patients with EoE, symptoms, endoscopic findings, and histologic features should all be considered.	100
18. When assessing disease activity in patients with EoE, the peak eosinophil count should be interpreted in the context of other histologic features, endoscopic findings, symptoms, and mechanisms of treatments being used.	100
19. When assessing disease activity in patients, symptoms of dysphagia cannot be considered in isolation, and should be interpreted in the context of food avoidance, modification of eating behaviors, and whether dilation has been performed.	100
20. In adult patients with EoE, endoscopists should have a high level of suspicion for the presence of a stricture.	96
21. In all patients with EoE, providers should recognize that endoscopic detection of strictures or narrowing is not sensitive.	96
22. Assessment of esophageal diameter in any patient with EoE can be achieved with esophagography, functional luminal impedance planimetry, or "sizing" techniques with balloon or bougie dilators.	84
Disease monitoring	
23. In patients with EoE, monitoring intervals to assess initial treatment response vary by treatment, with intervals of 6-8 weeks for diet elimination, 8-12 weeks for proton pump inhibitors and topical steroids, and up to 24 weeks for biologics.	92
24. During monitoring endoscopies for all EoE patients, providers should use the same biopsy protocol as for EoE diagnosis and obtain a total of at least 6 esophageal biopsy specimens from at least 2 different esophageal levels.	100
25. Monitoring endoscopies after a change in medical therapy should be performed at an interval sufficient to allow for washout from the prior treatment and evaluate efficacy of the new treatment on its own.	92

(continued on the next page)

TABLE 1. Continued

Statement	Percent agreement*
26. Less invasive modalities for assessing disease activity in patients with EoE, including unsedated transnasal endoscopy, a string-based collection device, and a sponge or balloon collection device, can be considered depending on local expertise and availability of these modalities.	96
27. Less invasive modalities for assessing disease activity should not be used for patients who may need esophageal dilation or for initial diagnosis.	96
28. Structured clinical and endoscopic monitoring should be implemented to avoid gaps in care that increase the risk of fibrostenosis in patients with EoE.	96

EoE, Eosinophilic esophagitis.

*The criterion used for acceptance of a statement was a score of 7 to 9 on a 1-to-9 scale of acceptance from at least 80% of the voters.

duodenal biopsy specimens is relatively low in EoE patients,⁵³⁻⁵⁶ but if obtained in the setting of suspected non-EoE EGIDs, 1 study suggests that up to 8 gastric and 4 duodenal biopsy specimens are required to maximize the sensitivity of detecting EGIDs.⁵⁷

5. In children with known EoE, biopsy specimens obtained during monitoring endoscopies can be limited to the esophagus if prior gastric and duodenal biopsy specimens were normal, the stomach and duodenum appear normal, and there are no new symptoms to suggest gastric or small intestinal pathology.

Endoscopic assessment of the esophagus through direct visualization and biopsies is recommended as a mainstay of monitoring for improvement and/or progression of disease activity in children known to have EoE.^{4,7,58} Although endoscopic biopsies are generally safe,^{59,60} they do involve rare but inherent risks, including bleeding, infection, and perforation.⁶¹ As such, routine biopsies of the stomach and duodenum during procedures performed for disease monitoring of EoE, in the absence of other indications and/or concerning findings, are relatively low yield and may add unnecessary patient risk, cost, anesthesia duration, and burden.^{7,53,58,62}

6. Providers should document the EREFS in all children undergoing endoscopic procedures with suspected or known EoE to allow for initial and longitudinal assessment of endoscopic severity.

Providers should document the EREFS^{63,64} during all endoscopic procedures in children with suspected or known EoE to enable both initial assessment and longitudinal tracking of disease severity.^{4,17,65} EREFS evaluates key endoscopic findings—edema, rings, exudates, furrows, and strictures—and correlates closely with histologic disease activity in children and adults.^{17,18,66} The most common scoring used clinically is to assess the overall worst finding in the esophagus, with a total score ranging from 0 to 9 (edema is present [1] or absent [0]; rings are mild [1], moderate [2], severe [3], or absent [0]; exudates are mild [1], severe [2], or absent [0]; furrows are mild [1], severe [2], or absent [0]; and strictures are present [1] or absent [0] with the esophageal diameter estimated in millimeters). The grades for all individual features should be reported at each

endoscopy, and a visual atlas in the endoscopy suite may be helpful as a reference to facilitate scoring. As demonstrated in several prospective studies, higher EREFS scores are associated with active disease in children, whereas a reduction in scores reflects treatment response.^{17,18,67} Incorporating EREFS into pediatric clinical practice provides a standardized and objective tool to monitor endoscopic changes over time and measure treatment efficacy.

7. In children with EoE, esophageal string testing and unsedated transnasal endoscopy (uTNE) should be reserved for monitoring disease status. Providers should not use either modality to establish an EoE diagnosis.

As patients undergo treatment for EoE, it is essential to ensure remission on therapy by esophageal sampling. Using standard sedated upper endoscopy for esophageal sampling with biopsies results in a cycle of repeated procedures and accumulated patient burden. There is additional concern for repeated exposures to anesthesia in pediatrics, and in 2016 the FDA issued a black box warning for anesthesia in children under the age of 3 years.⁶⁸ Although the data for this warning were based on animal studies that demonstrated repeated and prolonged anesthesia impacted brain development, the apprehension about the repeated anesthesia in human children remains.⁶⁹ Beyond concerns with anesthesia, the repeated endoscopic procedures have an impact on quality of life related to missed school, work, and social events, as well as high associated costs.⁷⁰⁻⁷²

uTNE and the esophageal string test (EST) are 2 less invasive modalities of sampling the esophagus that circumvent the need for anesthesia.⁷³ Despite collecting smaller biopsy specimens, uTNE accurately assesses disease activity as compared to traditional biopsies.⁷⁴ The EoE histologic scoring system can also be assessed on uTNE biopsies similar to standard biopsies.^{75,76} The uTNE procedure often requires <10 minutes to perform and patients spend on average 2 hours less time in the hospital than they do for a traditional endoscopy with anesthesia.⁷⁷ The main adverse events occurring with uTNE are vomiting/spitting up and epistaxis, although these do not prohibit completion of the study.⁷⁸ Use of virtual reality goggles with uTNE allows for

distraction from the procedure, with good parental and patient satisfaction with this approach due to lack of anesthesia and time savings.^{78,79}

The EST is a minimally invasive test whereby patients swallow a capsule attached to a string that dwells in the esophagus and absorbs inflammatory factors from the esophagus.⁸⁰ The end of the string is taped to the cheek for an hour before the string is removed and sent to a laboratory for analysis of the absorbed secretions of cytokine and eosinophil-derived proteins that correlate with disease activity. These include major basic protein (MBP), eosinophil-derived neurotoxin, Charcot-Leyden crystal protein/galectin-10, eotaxin-3, and eosinophil peroxidase.⁸⁰ Statistical modeling has shown that eotaxin-3 and MBP measurements combined can accurately predict histologic disease activity on esophageal biopsy.⁸¹⁻⁸⁴ Overall, patients are satisfied with the EST, with 98% of children and 96% of adults willing to use this methodology again for EoE surveillance, and 74% of children preferring EST to standard endoscopy with anesthesia. Rare adverse events include gagging, sore throat, or vomiting.⁸¹

Although EST and uTNE have been both validated in pediatric EoE cohorts and shown to detect disease activity, these modalities cannot provide a global assessment of disease activity or fully address the differential diagnosis of EoE at initial evaluation. For example, EST cannot assess for endoscopic findings or fibrostenotic changes in the esophagus, and with severe fibrostenosis the capsule may not be able to be swallowed. Because the transnasal scope is only 3 to 5 mm in diameter depending on the model used, it may not detect strictures that require dilation and video resolution is lower than with standard scopes. Not all transnasal scopes easily allow for assessment and sampling from the stomach and small bowel. As such, if EoE is suspected, standard sedated upper endoscopy with biopsies should be performed initially to fully assess for disease, esophageal caliber, and other potential causes of the clinical presentation. Subsequently, if a patient does not have concern for esophageal strictures or a narrow-caliber esophagus, noninvasive methods for follow-up may be considered. Currently, the role of uTNE or EST in screening for EoE in high-risk populations has yet to be determined and data are currently lacking, but may be a future application of these less invasive technologies.

8. In children with EoE, esophageal dilation can be considered in patients with symptomatic strictures or narrow-caliber esophagus on esophagram or endoscopy regardless of disease activity.

A stricture leading to dysphagia or recurrent food impactions is a severe consequence of chronic inflammation in EoE. Esophageal narrowing results in dysphagia as well as meal-time coping strategies such as over-chewing and lubricating foods for easier swallowing.⁸⁵ Strictures and esophageal narrowing are less common in the pediatric

population compared to adult patients. However, there are children who develop strictures, narrowing, and fibrostenotic symptoms early in life, and these can be hard to detect on endoscopy compared with esophagram.⁸⁶ Although controlling inflammation is paramount to preventing future development of strictures,^{24,72} dilation allows for immediate relief from dysphagia symptoms.⁸⁷⁻⁸⁹ Esophageal dilation has been shown to be safe and effective in both children and adults with EoE.⁹⁰ A systematic review of 845 patients, which included 87 children, demonstrated safety and efficacy, with more than 95% reporting symptom improvement.⁹¹ In the largest single-center case series to date of 68 EoE pediatric dilations, no perforations or significant hemorrhages were reported, and 14.7% of patients reported postprocedure pain.⁹² The patients in this cohort could have either active disease or be in remission at the time of dilation, and there was no difference in adverse events by level of disease activity. Therefore, dilation in symptomatic pediatric patients can be considered at the time of initial endoscopy to address a detected stricture or delayed until after treatment to see if the stricture improves after inflammation is controlled and if symptoms persist. In either case, practitioners should consider dilation as an adjunct therapy in children with EoE-related esophageal strictures to reduce symptoms, prevent food impaction, and improve eating behaviors.

9. Fluoroscopic imaging of the esophagus may be appropriate for evaluating children with dysphagia but should be recognized to have limited sensitivity and specificity for identifying strictures or determining esophageal caliber.

Dilation in the pediatric patient may require additional anesthesia and procedure considerations necessitating advanced planning. Thus, gathering information on esophageal caliber in patients with dysphagia or food impaction before endoscopic procedures can allow for optimal preprocedure decision making. In addition, endoscopic evaluation of the esophagus cannot always detect luminal narrowing. In a study of 22 children with EoE and esophageal stricture who had both esophagram and endoscopy, 12 patients (55%) were diagnosed only with esophagram, meaning that more than half of the strictures were missed with endoscopy alone.⁸⁶ Studies in adults have similar results, with endoscopy having just a 25% sensitivity (95% CI, 5.5-57.2%) for detecting ≤ 15 mm narrowing in the esophagus.⁹³ In 1 study of 48 adult patients who underwent endoscopy with endoluminal functional luminal impedance planimetry (EndoFLIP), 12 had a diameter of <15 mm not noted on endoscopy.⁹⁴ Use of a barium pill to assess retention in the esophagus has been cited as a means for increasing the sensitivity of esophagram in a small case series.⁹⁵ Despite some limited sensitivity as well as a minimal risk of radiation exposure, a barium swallow study should be considered in children in

the setting of ongoing clinical symptoms such as food impactions and dysphagia, and in conjunction with decision making before performing endoscopy.

10. Providers should consider initiating feeding therapy in children with EoE who have chronic feeding difficulties, taking into consideration inflammatory and fibrostenotic disease activity, specific dietary needs, and goals of feeding therapy.

Feeding difficulties in young children are a common presenting symptom of EoE, with a frequency of up to 17%.⁹⁶ Learned maladaptive behaviors are the most common feeding issues, noted in 94% of patients with EoE and feeding disorders and may include food refusal, refusal to try new foods, frequent meal time disruption, and requiring prompting to eat.⁹⁶ Other feeding issues that can be associated with EoE in children include lack of solid texture selections, altered oral sensory and motor skills, as well as developmental delay in gross and fine motor skills.⁹⁶

To help children overcome feeding obstacles, many clinicians consult a feeding therapist. Feeding therapy can involve multiple different formats depending on children's needs. Intensive feeding programs in particular may use a combination of speech pathology, occupational therapy, nutritional support, or psychology providers.⁹⁷ These multidisciplinary programs may meet multiple days per week with a goal of increasing the amount and types of food ingested by mouth. Intensive feeding programs may be challenging to implement in many children with EoE because of financial constraints, a need for insurance approval, geographic distance to feeding programs, and family difficulties with time requirements for program success.⁹⁸ Furthermore, intensive feeding programs are based on positive reinforcement, which may not be possible in the setting of active disease or fibrostenosis. Therefore, it is critical to address ongoing active EoE or esophageal narrowing to increase the effectiveness of feeding therapy, and consideration may be given to waiting to enroll in feeding therapy programs until biologic EoE disease activity is addressed.

Once feeding therapy has been initiated, if there is a plateau or a reduction in progress, it is important to assess compliance with EoE treatment and reassess inflammatory and fibrotic aspects of disease activity. For patients with delayed motor skills, there may be a desire to initiate speech or occupational therapy to develop fundamental feeding-related abilities, such as bringing food to the mouth or tolerating oral stimulation. However, it is crucial for gastroenterologists and allergists to collaborate closely with therapists in settings of ongoing disease activity in children, as advancing feeding therapy too aggressively with active EoE may be counterproductive.

11. Providers should carefully assess readiness and address preprocedure anxiety levels in older adolescents and young adults before performing either sedated or unsedated endoscopic procedures.

Retrospective studies of endoscopy have shown a high level of comorbid anxiety and depression in the EoE population.⁹⁹⁻¹⁰¹ Adult patients in particular have been noted to have increased esophageal hypervigilance as a driver of symptom burden.¹⁰² However, there are few data regarding health-related quality of life and stressors in adolescent and young adult populations with EoE.¹⁰³ Patients newly diagnosed with EoE may have increased symptom burden and anxiety, whereas children with neurocognitive differences (eg, attention deficit and hyperactivity disorder and autism) may be at risk for increased anxiety, sleep disturbance, and lower quality of life.

Practitioners should understand that the increased procedure burden required for EoE patients affects quality of life. Additionally, at the outset of disease, patients often have more endoscopies at the time when they may have the most anxiety and stress. Studies have shown that patients on diet elimination therapies who require more frequent endoscopies than patients on medical therapy have decreased quality of life.¹⁰⁴ The stressors of increased endoscopies include fear of intravenous line placement, postprocedure pain, and situational stressors such as missing school and sports. Understanding these stressors and attempting to mitigate some of these issues can begin to ease the disease burden. For example, considerations for a needle-phobic patient include use of numbing cream, inhalation anesthesia for induction, or uTNE. A patient with school-related stress may be able to defer a procedure to school breaks or summer vacation.

12. Providers should implement a structured transition plan from pediatric to adult care in patients with EoE.

Eosinophilic esophagitis is a chronic disease and lapses in care are associated with increased risk of fibrostenosis.¹⁰⁵⁻¹⁰⁷ Unfortunately, adolescents transitioning from pediatric to adult care are at a high risk for noncompliance and loss to follow-up¹⁰⁸ and only a minority of patients receive support during this transition.¹⁰⁹ A survey study of teens with EoE/EGID and their parents found that 78% and 76%, respectively, had no knowledge of health care transition.¹¹⁰ Although paradigms have been proposed for transition in EoE, few are implemented.¹¹¹⁻¹¹³

One study that tracked adolescents as they transitioned from pediatric care to adult providers found a 16% loss to follow-up rate.¹¹⁴ Patients had on average 299 days from their pediatric visit to their adult visit and 790 days in between procedures. In addition, rates of symptoms and medication nonadherence were increased in the population after transition, underscoring the importance of establishing care.¹¹⁴

To decrease loss of follow-up for EoE patients, providers should have detailed and proactive discussions with adolescents and young adults, as well as their caregivers, about the transition period. Physicians should discuss items such as how to call and make appointments on their own, how to send medical records to new

providers, and what will happen with their new doctor. An expanding literature outlines these and other components of effective pediatric-to-adult transition programs, but formal programs are still uncommon in EoE.^{111,112}

Disease assessment

13. In a patient with suspected EoE, the initial EGD should be performed off treatment.

Eosinophilic esophagitis is best diagnosed when the initial upper endoscopy is performed off therapy that could potentially obscure a diagnosis.⁴ The corollary is that in patients who are strongly suspected to have EoE (eg, food impaction, multiple atopic conditions, family history) but who have an endoscopy and biopsy that is “negative,” potential confounders including medications (proton pump inhibitors [PPIs]) and inhaled or intranasal steroids), dietary avoidance, seasonality, and inadequate biopsy sampling should be investigated. It is important to establish a definitive diagnosis of EoE off treatment for several reasons. Proof of diagnosis has important implications including the need for lifelong therapy and monitoring, the need to assess for strictures, and the potential for treatments that would be ill advised without a clear diagnosis. Although empiric therapy for a suspected diagnosis of EoE can be easy and safe to apply, it should be avoided until the diagnosis is confirmed. For example, PPIs or milk elimination leads to disease resolution in 40% to 50% of patients.¹¹⁵⁻¹²⁰ A response to PPIs, however, will not differentiate if the underlying process is EoE, gastroesophageal reflux disease (GERD), or both.¹²¹⁻¹²³ Additionally, an initial EGD before EoE therapy (understanding that some confounders such as inhaled steroids for asthma generally cannot be stopped) would allow for assessment of a symptomatic stricture requiring esophageal dilation, thereby avoiding the wait for empiric medical therapy to become effective in improving stricture diameter.

There are clinical challenges related to approaching a patient with suspected EoE who has been started on empiric PPI therapy for symptoms thought to be GERD (eg, heartburn, chest pain; empiric PPI therapy is not indicated for dysphagia symptoms alone). It is recommended that all patients stop medical therapy before endoscopy, not only for possible EoE but also for unproven GERD per Lyon 2.0 recommendations and other guidelines.^{124,125} Although the time off medication required to attenuate the beneficial effects of previous therapy is unclear for EoE, evidence suggests for PPI therapy it may be at least 1 to 2 months. If empiric PPI therapy cannot be stopped because of patient intolerance, endoscopy can be performed, and if active EoE is present, PPI nonresponse can be confirmed. If EoE is not found, it would make sense to stop PPI treatment in the future to confirm or refute the presence of EoE. Starting diet and/or steroid therapy in a patient with suspected EoE before confirming a diagnosis is not recommended.

14. In a patient with suspected EoE, a standard EGD should initially be performed to allow for comprehensive assessment (including gastric and duodenal biopsies when indicated) and esophageal dilation of a symptomatic stricture if needed.

A standard endoscopic examination as opposed to less-invasive testing (also see statements 7, 26, and 27) should be performed for several reasons for initial assessment of suspected EoE. Multiple studies have demonstrated that symptoms may underestimate disease severity because of patient accommodation and eating behavior modifications.¹²⁶⁻¹³¹ As a result, a critical stricture that has or could lead to food impaction may be present even if symptoms do not appear to be prominent.^{132,133} Dilation cannot be performed with uTNE, and detection of strictures may be inferior with uTNE, because the scope may not be able to fully expand the esophageal lumen and the very narrow scope diameter cannot be used to gauge esophageal diameter; sponge- or string-based assessments also cannot assess for strictures.⁷⁸ It is also unclear how well EREFS can be assessed with uTNE as compared to standard endoscopy.^{64,134} Moreover, the differential diagnosis for suspected EoE includes many upper GI conditions, and a standard endoscopy will permit a thorough examination not only of the esophagus but of the stomach and duodenum, and for biopsies in all locations (including to evaluate for more distal eosinophilic disease when indicated).^{54,135}

15. All patients who have symptoms or endoscopic findings consistent with EoE should have esophageal biopsy specimens obtained.

Esophageal biopsy specimens should be obtained at endoscopy for several reasons. First, biopsies are required to obtain tissue for the histologic assessment needed for diagnosis of EoE^{2,4} and to guide and monitor subsequent long-term treatment to prevent worsening symptoms and progression to stricture formation.¹³⁶⁻¹³⁹ Second, other esophageal diseases can manifest with dysphagia and have similar endoscopic findings. For example, esophageal scarring diseases such as lichen planus or lymphocytic esophagitis may occur in any part of the esophagus with rings and strictures, and biopsies are required to distinguish this and other endoscopic mimics of EoE from EoE itself (Fig. 2).¹⁴⁰⁻¹⁴⁶ Esophageal strictures should also be biopsied to assess etiology, and in EoE the most common location is in the distal esophagus, which can overlap with GERD findings.¹⁴⁷ Third, patients with EoE, particularly children, may have a normal esophageal appearance such that the diagnosis can only be made with esophageal biopsy.¹⁴⁸⁻¹⁵¹ Fourth, findings on biopsy may not only confirm the diagnosis but suggest a more fibrotic phenotype of EoE with the presence of lamina propria fibrosis and histologic features of disease chronicity.¹⁵²⁻¹⁵⁴ Assessment of lamina propria fibrosis and basal zone hyperplasia are now incorporated in the Index of Severity for EoE (I-SEE) and should be assessed for

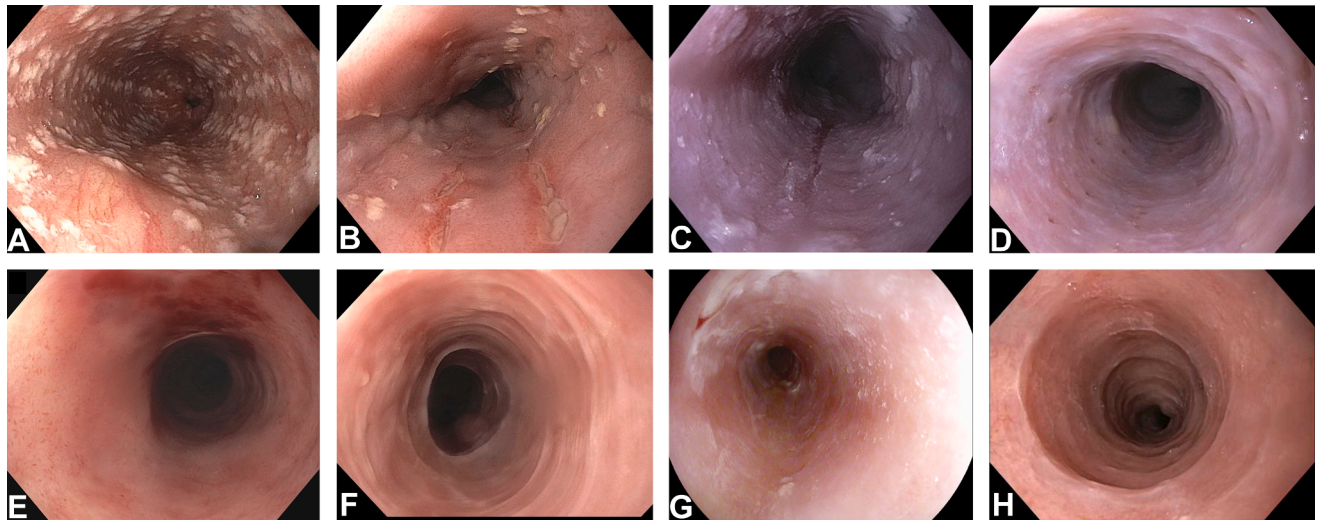


Figure 2. Examples of endoscopic mimics of EoE are shown and include esophageal candidiasis (A), Crohn's esophagitis (B), esophagitis dissecans (C), and pseudodiverticulosis (D). Lichen planus can have a range of findings such as edema and crepe-paper mucosa (E), rings (F), and narrowing and exudates (G). Lymphocytic esophagitis can also mimic EoE (H). *EoE*, Eosinophilic esophagitis.

initial and follow-up disease severity determination.¹⁵⁵⁻¹⁵⁸ (Also see statement 24 for additional discussion of esophageal biopsies.)

16. The definitive role of functional luminal imaging planimetry in the routine care of patients with EoE has yet to be determined.

Endoluminal functional luminal impedance planimetry (EndoFLIP) has the potential to add complementary information for assessing the severity remodeling in EoE.^{159,160} For example, the unique ability of EndoFLIP to assess esophageal wall dynamics, including compliance and distensibility, cannot be measured with any other test. It is more sensitive than endoscopy alone for detecting esophageal strictures and may help the endoscopist more specifically target strictures that require dilation.¹⁶¹⁻¹⁶⁶ Abnormal findings on EndoFLIP may also explain the presence of persistent dysphagia despite successful histologic response and in an otherwise normal-appearing esophagus¹⁶⁷ and predict the occurrence of a food impaction independent of other modalities.¹⁶⁸ Measurement of esophageal motility patterns in combination with lumen characteristics may provide prognostic and therapeutic information¹⁶⁹ and can be an additional measure to follow longitudinally in response to therapy.^{89,170}

Nevertheless, use of EndoFLIP requires availability of the device itself, additional expense, additional procedure time, and substantial operator and endoscopy staff expertise, which may not be practical for all gastroenterology units. Furthermore, endoscopists experienced with esophageal dilation, whether with bougie dilators or using the balloon pull-through technique,^{133,171,172} may adequately assess the presence of strictures and determine the esophageal lumen diameter by the sensation of resistance on passing the dilator or visible dilation effect. In skilled hands, dilation with these techniques may be both a diag-

nostic and therapeutic substitute for EndoFLIP albeit without precise measures of esophageal distensibility.¹⁷³ Although a formal consensus on the optimal approach to performing EndoFLIP for suspected esophageal motility disorders has been published,¹⁷⁴ an analogous document has yet to be released specifically for EoE although efforts are under way. In addition, normative values of the esophageal diameter for young children are lacking. Because of its evolving role, routine use of EndoFLIP is not currently recommended in all EoE patients.

17. When assessing disease activity in patients with EoE, symptoms, endoscopic findings, and histologic features should all be considered.

Multiple studies have shown that symptoms only modestly correlate with endoscopic and histologic disease activity in EoE, and because of that, symptoms cannot be monitored in isolation for EoE.^{4,126,155,175} The discordance of symptom and biologic metrics of endoscopic and histologic disease activity can be understood in several ways.^{131,176} Symptoms can be minimized with adaptive eating behaviors or if esophageal dilation is performed, although biologic activity persists.^{128,129,177} Conversely, symptoms can persist despite effective treatment of inflammation in the presence of strictures or narrowing that are either unrecognized or not dilated, esophageal hypersensitivity or hypervigilance, superimposed esophageal dysmotility, or an infection such as Candidiasis complicating treatment.^{86,93,94,102,178-184} Given the patchy nature of EoE, there may also be ongoing inflammation that is missed, particularly if not enough biopsy specimens are obtained, or with subepithelial inflammation if lamina propria tissue is not obtained on biopsy.^{50,51,185,186} With endoscopic assessment, it is also important to distinguish inflammatory (exudates, furrows, edema) from fibrotic (rings, strictures) features of EoE. With short-term treatment, one could

expect resolution of the former but not the latter. The extent of esophageal involvement may also be important, but data are mixed.¹⁸⁷ Thus, although symptom improvement is a goal of EoE treatment, it should be accomplished in conjunction with endoscopic and histologic improvement, so all 3 domains should be considered when assessing disease activity.

18. When assessing disease activity in patients with EoE, the peak eosinophil count should be interpreted in the context of other histologic features, endoscopic findings, symptoms, and mechanisms of treatments being used.

EoE is a Th2 immune-mediated disease with multiple cell types, including eosinophils, basophils, lymphocytes, mast cells, and fibroblasts, and cytokines involved in pathophysiology and leading to disease manifestations.^{188,189} Eosinophil density on esophageal biopsies has traditionally been the diagnostic reference standard of the disease, but likely represents an oversimplification of disease activity.^{175,190} Recent clinical trials of the eosinophil depleting agents liren-telimab and benralizumab highlight this issue; use of both led to high rates of histologic response, as measured by esophageal eosinophil counts, but no improvement in symptoms or endoscopic end points.^{191,192} As such, it is now apparent that more comprehensive, validated measures of disease activity should be considered when assessing response to therapy in EoE. These include the EoE histologic scoring system, which incorporates 8 histologic disease features, only 1 of which is eosinophil density, and EREFS, which provides a global endoscopic measure of disease activity.^{63,193} The newly described clinical severity scoring system (I-SEE) also provides a standardized tool to measure global disease severity based on symptoms, adverse events, endoscopic and histologic features of inflammation and fibrosis, and is readily available as a downloadable app.^{155,194,195} Mechanism of action of treatment intervention should also be considered. For example, emerging agents that target mast cells or fibrosis may not impact eosinophil density but may still improve disease activity.

19. When assessing disease activity in patients, symptoms of dysphagia cannot be considered in isolation, and should be interpreted in the context of food avoidance, modification of eating behaviors, and whether dilation has been performed.

EoE patients typically develop a variety of behavioral coping strategies to avoid symptoms of dysphagia that falls within the rubric of “IMPACT” modifications where patients may Imbibe fluids, Modify foods, Prolong mealtime, Avoid hard textures, Chew excessively, and Turn away from tablets and pills.¹³¹ As above, there is only a modest relationship between endoscopic and histologic measures of disease activity with validated patient-reported outcome measures.¹²⁶ There is further disassociation of endoscopic and histologic disease activity measures and symptoms in the setting of esophageal dilation given that dilation

improves symptoms without affecting disease pathophysiology.^{88,128,129,196} Esophageal hypervigilance and anxiety may also explain ongoing symptoms and may be more important than traditional endoscopic and histologic measures of disease activity,¹⁰² which can also be seen when EoE and symptoms of avoidant restrictive food intake disorder overlap.¹⁹⁷

20. In adult patients with EoE, endoscopists should have a high level of suspicion for the presence of a stricture.

Left untreated, eosinophilic esophagitis progresses from an inflammatory to fibrostenotic phenotype in a time-dependent manner in most, but not all, patients.¹³⁶⁻¹³⁹ Moreover, the prevalence of strictures in EoE has increased steadily over the past 2 decades, with strictures estimated to occur in approximately 25% of adults with EoE.^{147,198,199} However, predicting the presence of strictures before endoscopy and detecting them at the time of endoscopy are challenging to accomplish reliably.^{86,93,94,200} A recently described model to predict fibrostenosis at the time of endoscopy found 5 easy-to-obtain clinical factors (age >18 years, symptoms for >5 years before diagnosis, dysphagia, food impaction, and lack of abdominal pain) were associated with strictures or narrowing at the time of endoscopy.²⁰⁰ As such, a high level of suspicion of strictures is warranted, especially in adult EoE patients with dysphagia or adaptive eating behaviors. (Also see statement 16.)

21. In all patients with EoE, providers should recognize that endoscopic detection of strictures or narrowing is not sensitive.

Detection of narrowing or strictures at the time of endoscopy is challenging, in part due to the small caliber of adult endoscopes coupled with the wide field of view from the endoscopy camera. Accordingly, strictures are the least reliably assessed feature of the EREFS.⁶⁴ Studies in both children and adults find that esophageal narrowing may be missed at the time of endoscopy and that endoscopy has a low sensitivity when compared to barium esophagography.^{86,93} The sensitivity of even endoscopically detecting a stricture of 13 mm or less is only 33% compared with esophagram.⁹³ Furthermore, esophageal narrowing not seen at the time of endoscopy may be detected by EndoFLIP.⁹⁴ (Also see statements 9 and 16.)

22. Assessment of esophageal diameter in any patient with EoE can be achieved with esophagography, functional luminal impedance planimetry, or “sizing” techniques with balloon or bougie dilators.

Determination of esophageal diameter in EoE is critical for selecting the appropriate size dilators to use in the setting of dysphagia and esophageal stricture. However, assessment of esophageal diameter at the time of endoscopy is problematic with poor interrater reliability for the determination of stricture diameter.⁶⁴ When compared to endoscopy in both adults and children, barium radiography is more sensitive for the detection of strictures, but the technique is also operator dependent.^{86,93} Barium studies may

be further optimized by use of barium tablets to estimate lumen diameter. Functional luminal impedance planimetry allows for accurate assessment of esophageal diameter at the time of endoscopy even in the absence of endoscopically determined narrowing, but incurs additional costs and may not be routinely available (also see statements 9 and 16).^{94,163,201} Detection of the point of initial mucosal disruption by either the esophageal balloon pull-through technique, sequential guidewire-based dilation, or bougie cap technique also allows for the determination of esophageal diameter.^{171,172,202} Opening a biopsy forceps may likewise provide information on luminal diameter as the tip-to-tip distance on the forceps is known, and retroflexion at the gastroesophageal junction can allow estimation of a distal stricture diameter as compared to the endoscope diameter. Additionally, a new technique uses a bougie-like cone-shaped plastic cap that is attached to the tip of the endoscope (available in sizes from 7 to 18 mm) and allows assessment of esophageal diameter in an inexpensive manner and direct visualization of the dilation, with an initial series reporting safety and efficacy.²⁰² In the clinical setting, any of these techniques can prove to be useful for assessing esophageal diameter, and the choice of the technique should be individualized to the patient or setting.

Disease monitoring

23. In patients with EoE, monitoring intervals to assess initial treatment response vary by treatment, with intervals of 6 to 8 weeks for diet elimination, 8 to 12 weeks for proton pump inhibitors and topical steroids, and up to 24 weeks for biologics.

An international expert group published recommendations for monitoring patients in EoE⁷; the rationale is that because the disease is chronic and in many cases progresses from inflammatory to fibrostenotic disease,¹³⁶⁻¹³⁸ it is important to monitor disease activity not just after initial treatment or after treatment changes but also long term to detect potential loss of response to therapy.²⁰³⁻²⁰⁸ Domains for monitoring include symptoms, endoscopic findings, and histologic features.^{131,176,209} The data to support specific intervals for initial treatment come from the known mechanism of action and time of onset of different treatments, and are supported by when follow-up was performed in multiple studies, including clinical trials. Therefore, initial diet elimination course is generally 6 to 8 weeks (not including the time it takes to initially start the diet after dietician or nutritionist consultation),^{118,119,210-212} PPIs are 8 to 12 weeks,^{115,116} and topical steroids are also 8 to 12 weeks.²¹³⁻²¹⁶ An additional caveat with diet elimination is that if there is initial improvement across domains of response but histologic response is not fully achieved, a longer initial course could be considered.²¹⁷ Assessment of response to a biologic such as dupilumab typically takes place at 24 weeks,^{67,218,219} but earlier monitoring can be performed in patients with more severe disease or in patients who require more frequent dilation, and response has been

shown earlier than 24 weeks as well.^{67,170,220,221} Thereafter, intervals for longer-term follow-up for all therapies depend on treatment response and individual patient characteristics, past adverse events, and disease severity.⁷

24. During monitoring endoscopies for all EoE patients, providers should use the same biopsy protocol as for EoE diagnosis and obtain a total of at least 6 esophageal biopsy specimens from at least 2 different esophageal levels.

A goal of performing surveillance endoscopy, in addition to assessing endoscopic findings with EREFS^{18,63,66} and performing esophageal dilation if needed,^{90,222} is to obtain adequate esophageal Biopsy specimens samples to assess for eosinophil counts and other histologic findings that assess biologic outcomes for treatment response. Biopsy specimens should be taken using the standard “turn and suction” technique for the esophagus, and single bites should be considered to improve quality of the specimens.^{5,185} Prior studies have shown substantial patchiness of inflammation in the esophagus in EoE, including between biopsy samples and even between different high-power fields within biopsies.^{49,51,52,153,223} Studies in adults and children show that obtaining at least 6 biopsy specimens will maximize the sensitivity of detecting histologic findings, if they are present,^{46,47,50} and targeting active inflammatory findings (particularly furrows and exudates) can increase biopsy yield.^{49,224} This approach has been echoed in a number of guidelines,^{1,2,4} although endoscopists should recognize that exudates can be washed off or pushed off with scope advancement or dilator passage. Additionally, during post-treatment surveillance it is important to target any residual findings for biopsy, but interpret these in the overall context of esophageal involvement. If findings are present only in the midesophagus, either obtaining an additional set here or including the midesophageal location with the proximal sampling is a reasonable approach.^{48,49,223}

There are few data to suggest whether to divide esophageal biopsy specimens into different pathology jars (eg, 1 jar for distal and a separate jar for mid/proximal), so this is a matter of clinical context. With systemic therapy such as diet elimination, biologics, or PPIs, biopsy specimens could be combined (although some data suggest a differential effect by location with PPIs²²⁵). With topical therapy, there could be differential effect by esophageal level, so it may make sense to separate samples in that setting. If samples are not separated but endoscopic activity differs by esophageal level, this should be well documented in the endoscopy report to facilitate interpretation of biopsy results.

25. Monitoring endoscopies after a change in medical therapy should be performed at an interval sufficient to allow for washout from the prior treatment and evaluate efficacy of the new treatment on its own.

This recommendation reflects the concept that when performing a disease activity assessment (endoscopy, histology, and symptoms), providers should be sure that the effect they are seeing is that of the current treatment being tested. If a prior treatment had been stopped but the effect has not fully washed out, then the subsequent results may be difficult to interpret. For example, consider a patient who had complete response to a topical steroid, but wanted to try diet elimination. If the steroids that led to remission are stopped and diet elimination started immediately with follow-up endoscopy performed in 6 weeks, and if that endoscopy and biopsy were normal, it would not be clear if this reflected persisting efficacy from steroids or the effect of the diet therapy.

Although the idea is straightforward, each case may be different for treatment and timing, and data are relatively sparse. Data from dietary elimination studies show that EoE can recur histologically and endoscopically within 4 weeks or less after adding foods back.²²⁶⁻²²⁸ For topical steroids, about 50% of subjects have a recurrence in about 90 to 120 days based on natural history studies and randomized withdrawal studies.^{206,229-233} For dupilumab, the exact timing has not been studied in detail, but 4 to 6 months' washout may be required given the long half-life of the medication in steady state.²¹⁸ From a practical standpoint, if a PPI or steroid is stopped (after having induced disease remission) and new treatment started, the next endoscopy could be performed in 6 months, particularly if the patient has minimal symptoms and low concern for food impaction from a stricture. For diet, this could be 3 to 4 months, and for dupilumab it may require 6 to 12 months, but all intervals should be individualized for patient and disease features. This recommendation is more pertinent if there has been a complete or partial treatment response in the past, or if there is concern about combination therapy being more effective. If a treatment is not effective, however, a washout period is not needed because the EoE is already confirmed to be active.

26. Less-invasive modalities for assessing disease activity in patients with EoE, including unsedated transnasal endoscopy, a string-based collection device, and a sponge or balloon collection device, can be considered depending on local expertise and availability of these modalities.

Data are increasingly being reported on less-invasive techniques for monitoring EoE disease activity. A common theme is that less invasive techniques appear useful for assessing inflammatory disease activity but cannot replace endoscopy with dilation in patients with esophageal strictures or narrowing. An increasing number of sites in the United States, particularly pediatric centers, have implemented programs with uTNE based on a series of studies showing that it is safe, well-tolerated, yields both adequate esophageal visualization and sufficient histologic sampling, reduces overall costs of monitoring, and decreases time

commitments for patients and caregivers.^{74-76,78,79,234-236} Data also show that uTNE can be used successfully to monitor food reintroduction protocols in dietary elimination.²²⁸ (Also see statement 7.)

Similarly, the cytology sponge has been shown to correlate well with esophageal biopsies, and data show that it also has good utility for monitoring food reintroduction.²³⁷⁻²⁴¹ For this test, a capsule that encloses a spherical collection sponge and is attached to a string is swallowed, the capsule dissolves in the stomach, and the sponge is quickly removed as it collects an esophageal mucosal sample. The resultant tissue sample, about the size of a single biopsy, can be processed by a local pathology lab to report eosinophil counts. The esophageal string test collects markers of inflammatory findings with similar accuracy as endoscopic biopsies, and can also monitor disease activity over time.^{80,82,83,242} For this test, a weighted-capsule attached to a string is swallowed, and over the course of an hour collects esophageal secretions for the analysis. The string is removed and the esophageal section is sent to a central lab for processing followed by reporting of whether EoE is active or not based on eotaxin-3 and major basic protein levels in the string.

27. Less-invasive modalities for assessing disease activity should not be used for patients who may need esophageal dilation or for initial diagnosis.

If strictures or esophageal narrowing are present or suspected, or if esophageal dilation is required or a possibility, then traditional sedated upper endoscopy is needed. Neither sponge-, balloon-, or string-based collection devices allow therapeutics or assessment of fibrosis. A stricture may also impede passage or withdrawal of a sponge-based device. Moreover, the small channel in transnasal endoscopes does not allow for passage of a balloon dilator, and although it is possible to pass a wire through a transnasal scope, for patient comfort dilation with balloons and bougies is recommended during sedated procedures in nearly all cases (although we note self-dilation has been used for other non-EoE conditions in carefully selected patients^{243,244}).

28. Structured clinical and endoscopic monitoring should be implemented to avoid gaps in care that increase the risk of fibrostenosis in patients with EoE.

Although it is well known that longer diagnostic delay increases the risk for fibrostenosis before EoE diagnosis,¹³⁶⁻¹³⁸ there are also data that show that if patients are either untreated or have gaps in their care (including being lost to follow-up and then returning to care) after EoE diagnosis, they are also at risk for progression. Specifically, data show this progression to fibrostenosis in patients who had procedures canceled at the beginning of COVID and had their usual care delayed (ie, a natural experiment),¹⁰⁶ as well as in patients with a gap in care of 2 years or more, with increased rates of fibrostenosis the longer they are out of care.^{107,245} The corollary to these data are studies that show decreased need for

dilation or less fibrostenosis in both adult and pediatric patients who are well controlled with histologic response,^{24,25,246,247} or who have closer follow-up.²⁴⁸

Because of this, there are international expert recommendations for a structured follow-up program to be implemented in EoE, generally combining clinic evaluation with intermittent endoscopic assessment.⁷ The exact intervals will depend on a patient's prior course, treatment response, history of adverse events, need for dilation, and disease severity. However, the key point remains that symptoms do not correlate well with biologic disease activity in EoE (endoscopic and histologic findings) and that loss of response is possible even in patients without symptom recurrence.^{126,203,205,208,233} Therefore, endoscopic surveillance and/or some type of less-invasive esophageal mucosal sampling device, even in the absence of strong data providing definitive intervals, should still be considered and performed.

DISCUSSION

Because endoscopy is currently a key part of diagnosis and monitoring EoE, it is critical to have clear recommendations for the optimal approach to integrating endoscopy into clinical practice. The first set of guidelines for the endoscopic approach to EoE was published in 2022 and addressed topics of endoscopic diagnosis, grading, and dilation in detail, with only a brief discussion of monitoring.¹ Because of advances in the field and new topics to address related to endoscopy in EoE, a new consensus process with Delphi methodology was undertaken. Here, our expert multidisciplinary group reached agreement on 28 new statements across 3 main categories related to endoscopy: pediatric considerations, disease assessment, and disease monitoring. These include topics of when to suspect EoE and perform endoscopy in children, grading endoscopic severity using EREFS in children, esophageal dilation in children, and the role of less-invasive monitoring in children and adults. Additionally, we discuss performing the diagnostic endoscopy off treatment, the need to consider symptoms, endoscopic features, and histologic findings in parallel when assessing disease activity, treatment-based monitoring intervals, and the approach to esophageal biopsies during monitoring across all age ranges.

Taken together with the first set of ASGE endoscopic guidance statements, we now present a series of recommendations that reflect the optimal approach to endoscopy in EoE (Fig. 3). Endoscopy is initially performed when EoE is suspected based on clinical history. During the procedure, there should be a purposeful focus on the esophagus, with a careful examination on insertion, full insufflation and gentle washing of debris, and sufficient time taken to fully evaluate EREFS. Similarly, time should be taken to assess esophageal caliber and deter-

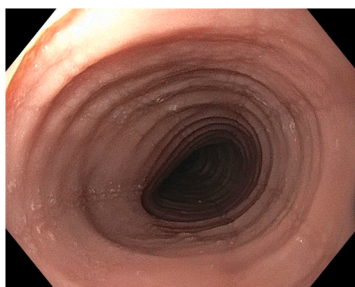
mine if dilation is needed using the approach detailed in the first ASGE guideline. Biopsy specimens should then be obtained using the turn and suction technique and collecting at least 6 biopsy specimens from across at least 2 esophageal levels, targeting active finding such as furrows or exudates if present. An approach such as this, where the esophagus is not just a waystation in the journey to the second portion of the duodenum, will ensure that all pertinent findings are detected, samples are obtained, and EoE disease activity is accurately assessed.

Despite the agreement across a wide range of recommendations, there are still many unknowns in the field of EoE, and future research is required to continue to expand our knowledge base to benefit our patients (Table 2). These include whether there is a role for artificial intelligence for endoscopic assessment; validating EREFS thresholds for treatment response; determining endoscopic predictors of response to treatment; identifying predictors of progression to fibrostenosis; understanding how uTNE, the string test, I-SEE, and EndoFLIP can best be used in practice; easing the psychologic burden of endoscopy and monitoring; how to more widely establish transition of care programs from pediatrics to adults; and how to best implement and optimize less invasive monitoring programs.

In conclusion, this new set of guidelines on the endoscopic management of eosinophilic esophagitis encompasses 28 statements on disease assessment, monitoring, and pediatric considerations. Coupled with the original 20 statements on the endoscopic approach to EoE, we have provided comprehensive and practical guidance for procedural-related aspects to the field. Although there are many questions still to be addressed, providers can use the data and approaches outlined here to provide high-quality endoscopic care to their patients with EoE.

DISCLOSURE

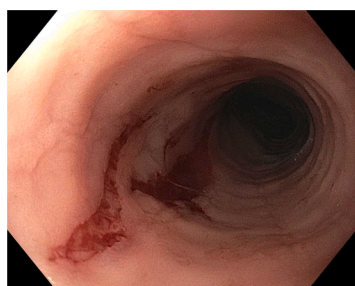
The following authors disclosed financial relationships: E.S. Dellon: Research funding from Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Celldex, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Sanofi, Shire/Takeda, and Uniquity; consultant for Abbvie, Adare/Ellodi, Akesobio, Alfa-sigma, ALK, Allakos, Amgen, Apogee, Apollo, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biocryst, Bryn, Calypso, Celgene/Receptos/BMS, Celldex, EsoCap, Eupraxia, Dr Falk Pharma, Ferring, GI Reviewers, GSK, Holo-clara, Invea, Knightpoint, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Sanofi, Shire/Takeda, Target RWE, Third Harmonic Bio, and Upstream Bio; and educational grant from Allakos, Aqilion, Holo-clara, and Invea. G.W. Falk: Consultant for Bristol Myers Squibb, Regeneron/Sanofi, Takeda, and EsoCap AG.



Optimal endoscopic view
E1, R2, Ex1, F1, S14

Examination:

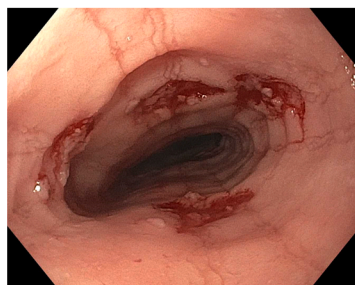
- Careful examination on insertion
- Fully insufflate
- Gently wash
- Take sufficient time
- Determine EREFS
- Search for stricture or narrowing



Good dilation effect

Dilation:

- Assess esophageal caliber
- Determine technique (balloon or bougie)
- Start low and go slow
- Underestimate initial size
- Reassess caliber by balloon or bougie resistance
- Look after each size to assess for adequate dilation effect



Biopsies targeting findings

Biopsy:

- At least 6 samples total
- Take from at least 2 esophageal levels (e.g distal and mid/proximal locations)
- Target active findings if present (exudates and furrows)
- Turn and suck technique

Figure 3. Optimal approach to endoscopy in EoE. *EoE*, Eosinophilic esophagitis; *EREFS*, EoE Endoscopic Reference Score, measuring Edema, Rings, Exudates, Furrows, and Stricture.

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TABLE 2. Future research directions for endoscopy in EoE

- Use of real-time AI for endoscopic assessment
- Validation of EREFS thresholds of response
- Endoscopic delineation of phenotypes
- Endoscopic predictors of treatment response
- Relation of inflammatory and fibrostenotic signs to treatment response
- Correlation of EREFS to non-eosinophil contributors to EoE such as mast cells, T cells, and fibroblasts
- Predictors of progression to fibrostenotic disease
- Utility of I-SEE in clinical practice
- Clarifying and establishing the role and methods of EndoFLIP for EoE in practice
- Optimizing clinical decision making on the need for endoscopic dilation
- Determination of preferred methods for esophageal dilation (balloon vs bougie vs cap vs EndoFLIP-assisted)
- Determination of the optimal biopsy technique in order to achieve a representative amount of subepithelial tissue
- Better elucidating the psychologic burden of EoE as related to endoscopy in children and determining methods to decrease stress related to EoE diagnosis and treatment
- Best ways to implement and support transition of care programs in EoE
- Evaluating and addressing barriers to care in EoE in the era of biologics
- Best ways to implement and support programs using less-invasive monitoring techniques in EoE
- Methods to detect fibrostenosis or remodeling on the esophageal string test
- Determination of the role of mucosal impedance monitoring in EoE
- Identifying optimal timing intervals for endoscopic re-evaluation once inflammatory remission is achieved

AI, Artificial intelligence; EndoFLIP, endoluminal functional luminal impedance planimetry; EoE, eosinophilic esophagitis; I-SEE, index of severity for EoE.

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; EGD, esophagogastroduodenoscopy; EGIDs, eosinophilic gastrointestinal diseases; EoE, eosinophilic esophagitis; EREFS, EoE Endoscopic Reference Score; EST, esophageal string test; GERD, gastroesophageal reflux disease; I-SEE, Index of Severity for EoE; MBP, major basic protein; PPIs, proton pump inhibitors; uTNE, unsedated transnasal endoscopy.

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