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Endoscopic approach to eosinophilic esophagitis: American Society for Gastrointestinal Endoscopy Consensus Conference

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Endoscopy plays a critical role in caring for and evaluating the patient with eosinophilic esophagitis (EoE). Endoscopy is essential for diagnosis, assessment of response to therapy, treatment of esophageal strictures, and ongoing monitoring of patients in histologic remission. To date, less-invasive testing for identifying or grading EoE severity has not been established, whereas diagnostic endoscopy as integral to both remains the criterion standard. Therapeutic endoscopy in patients with adverse events of EoE may also be required. In particular, dilation may be essential to treat and attenuate progression of the disease in select patients to minimize further fibrosis and stricture formation. Using a modified Delphi consensus process, a group of 20 expert clinicians and investigators in EoE were assembled to provide guidance for the use of endoscopy in EoE. Through an iterative process, the group achieved consensus on 20 statements yielding comprehensive advice on tissue-sampling standards, gross assessment of disease activity, use and performance of endoscopic dilation, and monitoring of disease, despite an absence of high-quality evidence. Key areas of controversy were identified when discussions yielded an inability to reach agreement on the merit of a statement. We expect that with ongoing research, higher-quality evidence will be obtained to enable creation of a guideline for these issues. We further anticipate that forthcoming expert-generated and agreed-on statements will provide valuable practice advice on the role and use of endoscopy in patients with EoE. (Gastrointest Endosc 2022;96:576-92.)

(footnotes appear on last page of article)

Eosinophilic esophagitis (EoE) is a chronic type 2 allergic inflammatory disease that is increasing in incidence and prevalence in both children and adults.[1] Endoscopy is a mainstay component of diagnosing and managing EoE. Esophageal mucosal biopsy sampling is essential for diagnosis and assessing response to treatment, whereas endoscopically scoring the disease uses visual assessment and the validated Endoscopic Reference System (EREFS). The EREFS, by using the 5 most common endoscopic findings in EoE (edema, rings, exudates, furrows, and strictures) is an important parameter for defining and monitoring disease activity.[2] In addition, management of esophageal strictures by endoscopic dilation should be recognized as a cornerstone of therapy for EoE, particularly in adult patients with untreated EoE who may be at risk for food impactions and/or present with esophageal strictures.[3-9]

Several evidence-based guidelines have been developed for EoE, including those published by the American Gastroenterological Association in collaboration with the Joint Task Force on Allergy/Immunology Practice Parameters,[10] the American College of Gastroenterology,[11] and a multisociety approach from Europe (United European Gastroenterology, European Academy of Allergy and Clinical Immunology, European Academy for Pediatric Gastroenterology, Hepatology and Nutrition, and European

Society of Eosinophilic Oesophagitis).[12] Generally speaking, these guidelines have focused on establishing definitions, diagnostic criteria, and best practices for medical management of EoE rather than on the role of endoscopy in ongoing patient care. This paucity of advice regarding indications and performance of endoscopic dilation, biopsy sampling, grading, and indications in EoE may reflect limited literature and clinical experience.[13]

To provide best practice guidance around applications of endoscopy and EoE, the American Society for Gastrointestinal Endoscopy convened a consensus conference to review all evidence and engage in a modified Delphi process. The Delphi process is a widely accepted means of formulating clinical guidance in medicine that has been successfully used by the American Society for Gastrointestinal Endoscopy and other GI societies, including in the areas of Barrett's esophagus,[14] questionnaires for and management of GERD,[15-17] protocols and metrics for pharyngeal manometry,[18] and EoE.[10]

METHODS

A modified version of the RAND/University of California, Los Angeles Appropriateness Methodology[19] was implemented to assess statements focused on the use of endoscopy in EoE. We used a modified Delphi process that included virtual on-camera discussions and revision of the statements, in addition to email discussions when needed. Voting was also performed both in person and through linked polls. A multidisciplinary team of international experts in EoE was recruited (Supplementary Table 1, available online at www.giejournal.org). Experts were chosen on the basis of extensive clinical experience with EoE patients, authorship on multiple peer-reviewed publications on EoE, participation in EoE clinical trials, and international recognition based on invitations to speak on EoE at major society conferences. These experts were chosen from multiple areas of medicine involved in the care of EoE including adult and pediatric gastroenterology, pediatric allergy, and therapeutic endoscopy. A physician expert in quality measures was also chosen to join the panel. Throughout the process, pertinent articles were identified and collected by a librarian with expertise in medical searches. These articles were collected and deposited in Covidence (Melbourne, Victoria, Australia). Searches were performed through Ovid MEDLINE and Cochrane Library and Embase using the search terms "eosinophilic esophagitis," "esophageal dilation," and "endoscopy" for the years 1993 to present, because the first report of EoE was published at that time.[20] The process is presented in Figure 1.

All online voting was performed through an emailed voting platform (SurveyMonkey, Momentive, San Mateo, Calif, USA, and Redmond, Wash, USA) after the meeting. The criteria used for acceptance of a statement were a score of 7 to 9 on a 1 to 9 scale of acceptance from at least 80% of the voters. The time from invitation of the experts to the finalization of accepted statements was between October 16, 2020 and June 11, 2021. Twenty statements achieved consensus (Table 1). Eight proposed statements that did not reach consensus are listed in Supplementary Table 2 (available online at www.giejournal.org).

RESULTS

Endoscopic diagnosis: biopsy

1. For the diagnosis of EoE, at least 6 biopsy samples should be taken from the esophagus for diagnosis of EoE. EoE is a patchy disease with considerable variability in the distribution of mucosal eosinophilic infiltration and other histologic findings such as epithelial hyperplasia, spongiosis, papillary height elongation, and eosinophil degranulation. Indeed, within the same patient, it is common to see esophageal eosinophil counts within both the normal and abnormal range. A number of studies in both pediatric and adult patients have investigated the optimal number of biopsy samples that need to be procured to increase the diagnostic sensitivity. In a series of 66 adults, the sensitivity of obtaining a diagnosis of EoE defined by >15 eosinophils per high-power field (eos/hpf) was 100% after obtaining 5 biopsy specimens compared with 55% with 1 biopsy specimen.[21] A pediatric study found that sensitivity of 2, 3, and 6 biopsy samples was 84%, 97%, and 100%, respectively.[22] Another series evaluated biopsy samples from the mid- and distal esophagus in 102 patients and found the probability of 1, 4, 5, and 6 biopsy samples yielding >15 eos/hpf was .63, .98, .99, and >.99, respectively.[23]

2. Biopsy samples should be taken from the distal and mid-/proximal esophagus for the diagnosis of EoE. It is recommended to take biopsy samples from multiple levels along the length of the esophagus and not in 1 location alone, ideally targeting areas of visible inflammation, if present.[21,24] This recommendation stems from the observation that histologic variability is common when comparing esophageal biopsy specimens within individual patients. In 1 adult series investigating the difference in eosinophilic infiltration between the proximal and distal esophagus, a higher density of eosinophilia was found in the distal esophagus than the proximal esophagus (mean, 82 eos/hpf vs 68 eos/hpf). This study showed that if only distal biopsy specimens were obtained, 100% would have been diagnosed; however, 20% of patients would have been missed if only proximal biopsy samples were taken. Biopsy sampling just below the upper esophageal sphincter is unlikely to demonstrate esophageal eosinophilia.[25] As a result, the location of biopsy samples in the proximal esophagus should be considered with this caveat. Further, it is unclear whether the proximal or mid-esophagus is more sensitive for EoE biopsy diagnosis. Whether biopsy

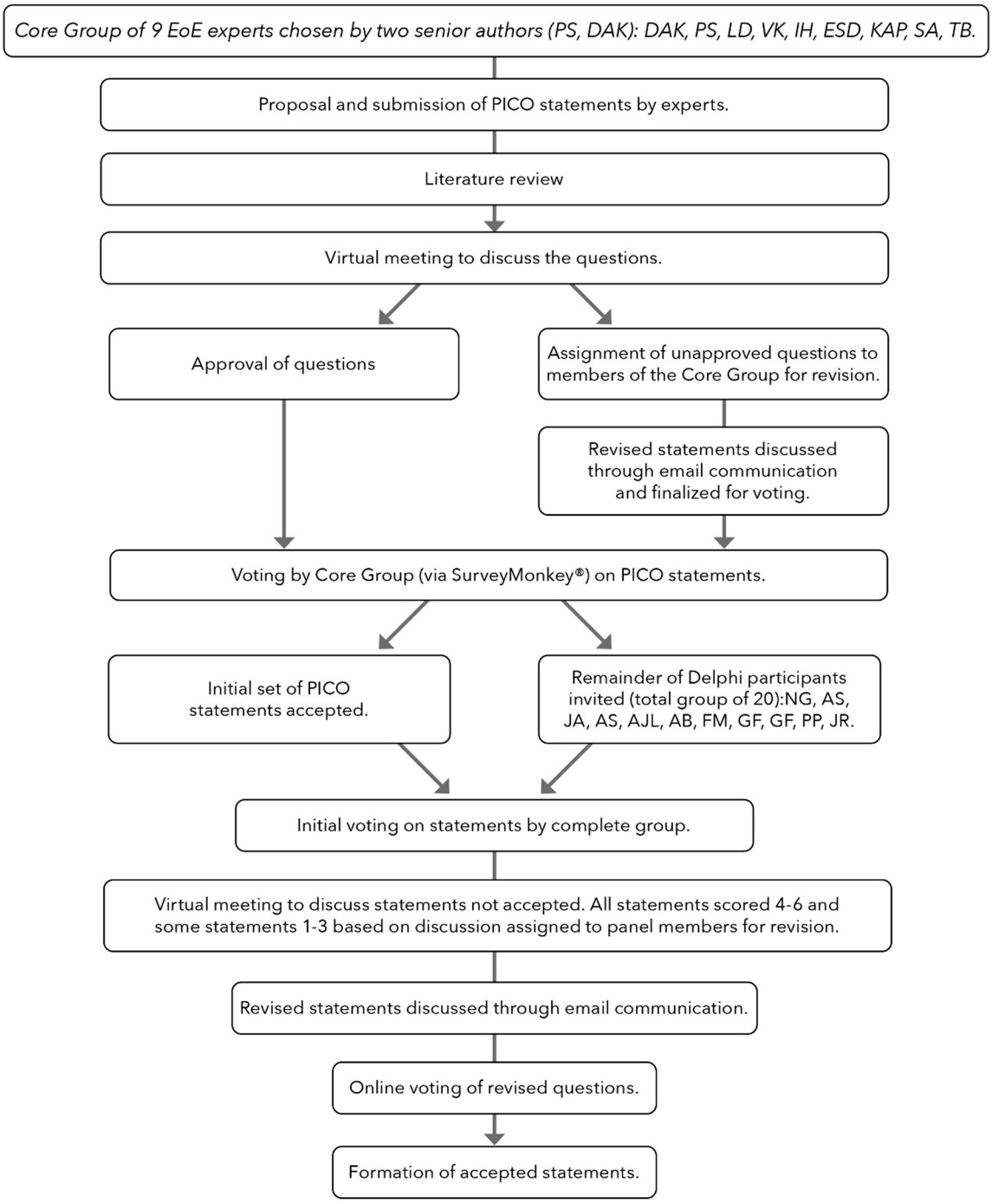


Figure 1. Modified Delphi process for the American Society for Gastrointestinal Endoscopy endoscopic approach for EoE consensus documentation. *EoE*, Eosinophilic esophagitis; *PICO*, Patient/Population/Problem, Intervention, Comparison, Outcome.

sampling should be performed in a 4-quadrant or variable level protocol has not been evaluated. There was also a failure to agree on whether biopsy specimens should be placed in 1 or multiple jars.

3. In a patient with suspected EoE, biopsy samples should be obtained from the esophagus regardless of endoscopic appearance. Although the presence of endoscopic features is common in EoE, eosinophilic infiltration can be found in biopsy samples of normal-appearing esophageal mucosa.[2,26] Specifically, a normal endoscopically appearing esophagus is seen in 10% to 32% of both pediatric and adult patients with EoE.[27,28]

TABLE 1. Endoscopic approach to eosinophilic esophagitis consensus statements

Endoscopic diagnosis
Biopsy
1. For the diagnosis of EoE, at least 6 biopsy samples should be taken from the esophagus.
2. Biopsy samples should be taken from the distal and mid-/proximal esophagus for the diagnosis of EoE.
3. In a patient with suspected EoE, biopsy samples should be obtained from the esophagus regardless of endoscopic appearance.
4. At the index endoscopy for EoE patients, multiple biopsy samples should be taken from the stomach and duodenum to assess for eosinophilic gastroenteritis in patients with compatible symptoms and/or endoscopic abnormalities.
5. Esophageal biopsy samples should be obtained at the time of food impaction if that is the initial presentation of suspected EoE.
Endoscopic grading
6. The EoE EREFS should be used routinely for assessing EoE activity during endoscopy.
7. In patients with suspected or established EoE, the EREFS applied to the highest scoring area should be used to assess the entire esophagus at each endoscopy.
8. In patients with EoE, an improvement in inflammatory features (ie, furrows, exudates, and edema) at each endoscopy is a desired endpoint of pharmacologic or dietary therapy.
Assessing response to therapy
9. Endoscopy and biopsy sampling, and not symptoms alone, are needed to assess EoE activity before and after any change in dietary elimination therapy or pharmacologic treatment.
Endoscopic dilation
10. Endoscopic dilation can be considered for all patients with EoE and an esophageal stricture with dysphagia.
11. The immediate endpoint of endoscopic dilation is the appearance of a mucosal disruption or reaching the target diameter.
12. In adult and adolescent patients with EoE, a goal luminal diameter that relieves dysphagia and food impaction (typically $\geq$16 mm) should be achieved over $\geq$1 sessions based on the initial caliber of the lumen and effect noted during dilation.
13. To lower the risk of perforation, achieving an esophageal luminal diameter of 16 mm may necessitate gradual dilation in >1 session of dilation.
14. Effective management of esophageal inflammation in patients with EoE and dysphagia attenuates the need for future endoscopic dilation.
15. In patients with EoE, different dilation techniques chosen on the basis of stricture characteristics and endoscopists' preference are acceptable for performing dilation therapy.
16. In patients with fibrostenosing EoE, dilation therapy should occur in conjunction with effective medical or diet elimination therapy for management of dysphagia.
17. In patients with fibrostenosing EoE with inflammatory activity, dilation can be done safely.
18. Empiric dilation may be performed for persistent dysphagia in the presence of a normal-appearing esophageal diameter by endoscopy and histologic remission achieved with medical or dietary therapy.
19. Most EoE patients with radiographically or endoscopically demonstrated perforation will respond to conservative therapy; endoscopic and surgical interventions are rarely needed.
Monitoring disease
20. In patients with EoE in remission, continued monitoring with symptoms should be performed. Consideration should be given to periodic endoscopy and biopsy sampling.

EoE, Eosinophilic esophagitis; *EREFS*, Endoscopic Reference System.

These studies include both pediatric and adult EoE cohorts. For example, in a study of 381 children with EoE, 32% of patients demonstrated a normal esophageal appearance on endoscopy.[28] Additionally, other studies examining the prevalence of EoE in adults with dysphagia found up to 46% of patients with EoE where the endoscopic appearance was described as normal on endoscopy.[29-31]

The sensitivity and specificity of typical endoscopic findings to diagnose EoE (in the 13 EoE patients identified in 1 study) was calculated to be 31% and 93%, respectively.[32] Additionally, in a large cohort of pediatric patients with food impactions, up to 38% had an esophageal endoscopic appearance described as normal or only erythematous.[33] Finally, 1 study failed to demonstrate significant differences in endoscopic findings when stratified by patient race with a normal esophagus described in 16% of whites and 32% of African Americans with EoE.[34] Three therapeutic trials further described that a normal endoscopic appearance was found frequently in enrolled subjects.[35-37] One concern, however, is that subtle esophageal findings of EoE may not be recognized by the less-experienced endoscopist, contributing to a false interpretation of a normal esophageal appearance. This is supported by endoscopic sensitivities of 95% to 100% in large cohort (88-318), multicenter, phase II and

III clinical trials that include prospective endoscopic assessment in adults.[37-39] Further, a high sensitivity in these trials was reported even when nonexpert practices enrolled subjects. Also, carefully done studies examining endoscopy performance have shown a sensitivity of more than 90% .[40-42] Because of the potential occurrence of a normal endoscopic appearance in EoE, particularly when endoscopy is performed by physicians with less experience in EoE, esophageal biopsy sampling should be performed in the absence of typical signs of EoE such as rings, exudates, or furrows if there is a clinical suspicion of the disease.

4. At index endoscopy for EoE patients, multiple biopsy specimens should be taken from the stomach and duodenum to assess for eosinophilic gastroenteritis in patients with compatible symptoms and/or endoscopic abnormalities. Non-EoE eosinophilic GI disorders (EGIDs) are substantially rarer than EoE. However, the occurrence of a non-EoE EGID concurrent with primary EoE can be present in patients initially believed to have consensus-defined isolated EoE. Conversely, esophageal eosinophilic inflammation can be seen in patients diagnosed with primary non-EoE EGIDs.[43] The clinical and biologic meaning of coexisting esophageal eosinophilia without typical findings or EoE is unclear. Nevertheless, because of the potential for multisegment GI eosinophilic disease with the potential that greater gut involvement would require treatment different from EoE, it is prudent to biopsy sample the stomach and duodenum at the time of initial or subsequent upper GI endoscopy for EoE if symptoms or endoscopic features are suggestive of a non-EoE EGID. These symptoms may include nausea, vomiting, and abdominal pain, whereas typical endoscopic findings of an EGID are erythema, nodularity, ulceration, or a normal appearance.[44] In addition, the concurrence of celiac disease and EoE has been reported, supporting the need to biopsy sample the duodenum when family history, symptoms, or endoscopic features are suggestive of potential celiac disease.[43-47]

Surveillance of nonesophageal GI segments in the absence of clinical or endoscopic features is of low yield. In adults, only 2.5% to 3% of patients with EoE who had extraesophageal biopsy samples were found to have eosinophilic gastritis, duodenitis, or celiac disease; most had symptoms and endoscopic features of extraesophageal disease.[48] This also applies to children with EoE in whom nonclinically indicated gastric and duodenal biopsy sampling at follow-up endoscopy yielded normal results or nonspecific features in most cases.[49] Note that this is in contrast to searching for a primary diagnosis of eosinophilic gastroenteritis where 62% of patients may have a normal endoscopic appearance.[50]

5. Esophageal biopsy samples should be obtained at the time of food impaction if that is the initial presentation of suspected EoE. Food impaction resulting from the effect of fibrosis on esophageal mural compliance and luminal diameter is a common initial presentation in children and adults with EoE.[51] Many patients will describe a history of intermittent or persistent dysphagia for weeks to years preceding the impaction and may have developed compensatory maneuvers during swallowing to avoid impaction. Careful questioning can elicit relevant information from the patient.[52,53] Others will remain asymptomatic between episodes of impaction.

It is necessary and appropriate for all patients who present for endoscopic removal of a food impaction (or other esophageal foreign body) to have a thorough examination of the esophageal mucosa away from the site of impaction.[54] Endoscopic features of EoE may be subtle or absent, and biopsy specimens are essential to establish the diagnosis.[55,56] Standard mucosal biopsy sampling of the distal and proximal esophagus should be obtained, avoiding the site of impaction (which may have acute local changes that could confound the histologic diagnosis) if possible. Failure to obtain biopsy samples at the time of impaction necessitates performing an additional endoscopy, which further delays confirmation of the diagnosis and medical treatment with the risk of losing these patients in follow-up.[57] Nevertheless, clinical situations such as patient instability or fear of aspiration during endoscopy may not allow the needed time to procure esophageal biopsy samples.

Endoscopic grading

6. The EoE EREFS should be used routinely for assessing EoE activity during endoscopy. The EoE EREFS provides standardized nomenclature and conveniently characterizes the 5 major endoscopic features of EoE: edema, rings, exudates, furrows, and stenosis (which also conveniently spells out "EREFS").[2] Inflammatory activity is demonstrated by the presence of edema, exudates, and furrows, whereas features of remodeling are assessed with rings and stricture. Fundamental limitations to the reliance on symptoms and histology for disease management are mitigated by incorporating a measure of endoscopic activity.[58,59] In children, symptoms can be nonspecific and include poor intake as well as avoidant restrictive food intake disorders, which may lead to an underappreciation of dysphagia. In adults, reports of dysphagia severity can also be affected by patient anxiety and hypervigilance and diminished by modifications to eating behaviors.[53,60-62] Moreover, relying on the peak eosinophil density for a clinical decision fails to account for the patchiness of microscopic activity and the importance of histologic abnormalities that can be driven by inflammatory cells and mediators other than the eosinophil.[63] Esophageal biopsy sampling also takes a small percentage of the EoE-involved esophageal mucosa and thus may not be an adequate gauge of global esophageal disease activity. Esophageal strictures because of rings, focal strictures, or diffuse luminal narrowing are not assessed by mucosal biopsy sampling; these gross findings provide information on disease severity, future risk of

food impaction, and decisions regarding esophageal dilation. Thus, endoscopic activity assessment complements histologic and symptom measures, providing a more comprehensive assessment of overall disease activity.

On a practical level, endoscopic assessment is easy and reliable, requiring little additional time during the performance of standard-of-care endoscopic procedures. U.S. and European studies have validated the inter- and intraobserver agreement with EREFS,[2,64,65] with a sensitivity and specificity of 90% in both pediatric and adult studies.[40,41] Further, the responsiveness of the EREFS to therapy has been demonstrated in numerous prospective and placebo-controlled clinical trials.[37-39] The nonsignificant changes in EREFS with placebo illustrate the objectivity of endoscopic assessment and contrast with the high placebo response for symptoms. Normalization of previously identified inflammatory features provides immediate, "real-time" information on the effectiveness of a medical or dietary intervention. These data also guide decisions on esophageal dilation in the presence of dysphagia and the absence of histologic activity assessment.

Clinical studies have variably separately scored activity in the proximal and distal esophagus and focused on edema and furrows. For clinical use, simplification of scoring (edema [absent or present], rings [absent, mild, moderate, or severe], exudate [absent, mild, or severe], furrows [absent or present], stricture [absent or present with estimation of diameter]) is suggested and incorporated into widely used endoscopic reporting systems. For simplicity, EREFS scores are sometimes annotated by the letters of the acronym followed by severity score (eg, Edema present, Rings moderate, Exudate severe, Furrows present, Stricture 10 mm becomes E1R2Ex2F1S10). Individual cases may benefit from additional qualifying statements regarding the extent of inflammatory features.

7. In patients with suspected or established EoE, the EREFS applied to the highest scoring area should be used to assess the entire esophagus at each endoscopy. Applying EREFS to the most affected area of the esophagus is most commonly used for data collection and to provide clinical reference points for immediate and longitudinal care of patients suspected of and those diagnosed with EoE. Although it has been used to assess different longitudinal segments of the esophagus as an independent measure, the positive correlation of mucosal eosinophilia with EREFS scores is consistent regardless of the segment assessed. In addition, measurement of the most affected part of the esophagus has been used successfully in both therapeutic and validation studies as a measure of clinical outcome. At this time, inadequate data are available to systematically compare the peak to the mean whole esophageal EREFS score to substitute the latter as a way to assess response to the therapy.

8. In patients with EoE, an improvement in inflammatory features (ie, furrows, exudates, and edema) at each endoscopy is a desired endpoint of pharmacologic or dietary therapy. Features within EREFS can be further divided into inflammatory (edema, exudates, and furrows) and fibrostenotic (rings and strictures) features.[39] This division is important because currently available EoE treatments, including proton pump inhibitors, swallowed or topical corticosteroids, and dietary elimination, are considered anti-inflammatory, with an initial primary goal of decreasing the esophageal eosinophilic infiltrate.[11,12] As a result, treatments aimed at reducing esophageal eosinophilia can be further assessed after an initial course of therapy by grading changes in the endoscopic inflammatory features. These are distinguished from esophageal dilation, which directly improves rings, strictures, and symptoms of dysphagia, but may not improve with acute treatment of inflammation.[66] Although some data indicate that medical and dietary therapy can improve fibrosis (seen histologically)[67-69] or esophageal caliber (as measured by the functional luminal imagine probe),[70] the preponderance of data is related to the decrease in eosinophilic inflammation and histologic severity.[71,72] Therefore, when assessing endoscopic features, seeing an improvement in edema, exudates, and furrows is an important visual clue that treatments are effective (eg, moving from pretreatment EREFS of E1R0Ex2F1S0 to post-treatment EREFS of E0R0Ex0F0S0).[73] In addition, of these inflammatory features, exudates correlate best with eosinophil counts on biopsy samples,[40,41,74] and observing improvement in the inflammatory EREFS features is a desired, important, and predictive endpoint of treatment.

Assessing response to therapy

9. Endoscopy and biopsy sampling, and not symptoms alone, are needed to assess EoE activity before and after any change in dietary elimination therapy or pharmacologic treatment. Eliminating or reducing esophageal eosinophilic infiltration to under the diagnostic threshold is an essential therapeutic goal in EoE. Normalization of inflammatory and possibly fibrotic features on histology and endoscopy is also an endpoint for clinical trials in EoE and provides an additional objective measure of therapeutic efficacy. Endoscopy with biopsy sampling should be considered in several circumstances: to evaluate a treatment regimen chosen to control symptoms and ideally resolve esophageal eosinophilia, after the institution of new treatments if the previous treatment failed, changes in symptoms or compliance with therapy,[75] and to identify specific food triggers that cause EoE in children[76,77] and adults.[78,79] Endoscopy with biopsy sampling should be repeated no earlier than 4 weeks after a change in diet therapy or 8 to 12 weeks for pharmacologic treatment to allow adequate time for a significant histologic change to occur.[11,12,71] The principle supporting the absolute need for endoscopy and biopsy sampling to assess medical therapy is guided by the poor correlation between histology and symptoms.

Patient reports of positive and negative symptoms have been repeatedly shown not to correlate with endoscopic or histologic evidence of disease remission. A number of standardized patient-reported outcome instruments have been proposed, but to date none has been found to be sufficient for predicting endoscopic or histologic remission.[80-85] These include the EoE Activity Index, a patient-reported outcome instrument that quantifies patient difficulties with dietary or behavioral modifications to facilitate the ingestion of different food consistencies[80]; the Dysphagia Symptom Questionnaire, a validated and reliable measure of dysphagia in patients with EoE that has been shown to correlate weakly, but significantly, with a change in peak eosinophil count in esophageal biopsy samples[83]; and the Pediatric EoE Symptom Score (v2.0), which includes 4 major domains: dysphagia, GERD, nausea/vomiting, and pain.[84] Several other studies have used nonvalidated instruments, which may contribute to inconsistent relationships between symptoms and esophageal inflammation in EoE patients.[86,87]

Although more accurate, the use of endoscopic features of EoE to assess therapy was also not endorsed by the panel as a primary endpoint of therapy. This is in part because endoscopic features of EoE are not pathognomonic and can be found in other esophageal conditions.[88,89] However, the expert group did note the value of the Endoscopic Reference Classification System that standardizes descriptions of most typical EoE endoscopic findings in 1 score.[29] The EREFS classification has been shown to have an adequate capacity to identify most patients with EoE,[40,41,90] but its performance is limited in determining response to treatment, with an area under the curve ranging from .79[89] to .88[40] when histologic remission was defined as a peak eosinophil count $\leq$15 eos/hpf. This means that the EREFS score misclassifies 12% to 21% of patients in terms of response to therapy. Therefore, the EREFS score should be used in conjunction with but not in place of histologic findings to accurately measure outcomes of treatment in EoE patients. Noninvasive or minimally invasive methods to assess disease activity are under development, and no peripheral markers currently predict the presence of inflammation in the esophageal tissue[91,92] or accurately differentiate EoE from other atopic diseases.[93]

Endoscopic dilation

10. Endoscopic dilation can be considered for all patients with EoE and an esophageal stricture with dysphagia. Dilation can be considered in all patients with EoE with dysphagia and an esophageal stricture, preferably in combination with medical and/or dietary treatment because dilation itself does not reduce mucosal eosinophilia. The effectiveness of esophageal dilation in patients with EoE has mainly been reported in retrospective, uncontrolled, single-center studies in which a proportion of the patients also used medical treatments for their EoE. A meta-analysis of these reports confirms that dilation is highly effective and safe, resulting in clinical improvement in 95% with perforation in .38% and need for hospitalization in .67%. Dilation was effective in patients with a diffusely narrowed lumen (small-caliber esophagus) or with single or multiple esophageal strictures. For example, esophageal dilation has also been reported to be highly effective for EoE patients with severe strictures <10 mm in diameter, with most achieving diameters of 15 mm or more.[94] The duration of clinical relief of dysphagia was variable. No differences have been reported according to the dilation device used in clinical series. A dilation-predominant long-term treatment strategy can be considered for symptom control in patients with a persistently symptomatic refractory stricture or as a temporizing measure at the initial or continued implementation of medical therapy.[95-98]

11. The immediate endpoint of endoscopic dilation is the appearance of a mucosal disruption or reaching the target diameter. No clear data-driven endpoints reliably define improvement in patient reports of dysphagia after esophageal stricture dilation. However, multiple studies have addressed technique, target diameter, and overall outcome.[95-98]

Potential factors that contribute to dilation success in EoE include predilation stricture diameter, location and extent of the fibrostenotic disease, presence of inflammation or fragility of the tissue, when moderate resistance is encountered during dilation, presence of blood on a dilator, and/or visualization of mucosal disruption. The bougie method allows for tactile feedback so the endoscopist may gauge when initial and moderate resistance is encountered as an endpoint. As the dilators are withdrawn, examining for heme may also indicate mucosal disruption, but the absence of heme does not exclude dilation effect.

Endoscopic visualization of mucosal disruption as an indication of adequate dilation is commonly seen after dilation with a through-the-scope balloon dilation or between passage of dilators should be expected and does not translate to an adverse event.[95-97,101] Instead mucosal disruption after dilation of an EoE stricture may signal that the endoscopist is at or near the goal for that dilation session. Deep rents or tears can be seen after dilations and may be associated with chest pain in up to 17% of patients.[96] It is important to forewarn the patient that some discomfort can be expected after the procedure and monitor for progression of symptoms such as worsening chest pain, shortness of breath, fevers, or chills that are indicative of perforation. It is also important to counsel the patient that more than 1 session of dilation may be required to improve symptoms, particularly in the presence of narrow strictures.[95 99,100]

12. In adult and adolescent patients with EoE, a goal luminal diameter that relieves dysphagia and food impaction (typically at least 16 mm) should be achieved over 1 or more sessions based on the

initial caliber of the lumen and effect noted during dilation. The clinical efficacy of esophageal dilation for EoE was summarized in a systematic review and meta-analysis by Moole et al.[97] Data were extracted from 14 studies (1607 patients) using esophageal dilation for EoE management. The pooled proportion of patients who showed clinical improvement with esophageal dilations after the median follow-up period of 12 months was 84.95%. In 2017, Moawad et al[95] published a second systematic review with meta-analysis of 27 studies that included 1820 esophageal dilations in 845 unique patients with EoE that suggested clinical efficacy.

Presently, there is a limited evidence basis for determining a target esophageal diameter (ie, 16-18 mm, etc). Nevertheless, 1 large cohort study of 207 adult EoE patients treated by esophageal dilation, in which mean esophageal diameter increased from 11 ± 3 mm to 16 ± 2 mm, was associated with a significant improvement in dysphagia.[66] Another study in 50 adult EoE patients treated with the BougieCap (Ovesco, Tübingen, Germany) correlated an increase in median esophageal diameter from 12 mm (interquartile range [IQR], 12-13) to 16 mm (IQR, 16-16; $P < .001$) and a decrease in median symptom severity (measured with the validated EoE Activity Index PRO instrument) from 32 (IQR, 27-41) to 0 points (IQR, 0-10; $P < .001$) at 2 weeks postdilation.[101] In another study, endoluminal functional lumen imaging probe diameters <17 mm were associated with higher risk of food impaction, lending support for a further targeted endpoint of 16 to 18 mm.[102]

Serial dilations and careful selection of the initial dilator size guided by repeated endoscopic inspections to look for tears are deemed to be safe practice methods.[5,103] When serial dilations are required, common practice is to not exceed dilation by >3 mm in a single dilation session.[4] This may necessitate multiple dilation sessions to attain a target esophageal diameter of 15 to 18 mm.[104]

13. To lower the risk of perforation, achieving an esophageal luminal diameter of 16 mm may necessitate gradual dilation in more than 1 session of dilation. Data suggest that perforation risk in EoE patients is low.[95-98] Dougherty et al[96] found in a systematic review and meta-analysis of 2034 dilations in 977 EoE patients that the estimated perforation rate was .033% (range, 0%-.226%) per procedure (9 perforations in 2034 procedures). None resulted in surgical intervention or mortality. Of note, 5 of 9 perforations described in studies of adult patients with EoE were published before 2009 (rate of .44% [range, 0%-2.75%]; after 2009, the pooled perforation rate was .030% [range, 0%-0.225%]), comparable with a .4% perforation rate cited for other benign causes of esophageal stricture.[105] Pooled data analyses also suggest that perforation rates with larger dilators (>17 mm) are 1.35% (95% confidence interval [CI], 0-8.43) versus .03% (95% CI, 0-0.226) for smaller dilators.[105] When compared with published experience using smaller dilators, larger dilators have also been more frequently associated with hospitalization and clinically significant chest pain. These data endorse the strategy to "start low and go slow," taking as many dilation sessions as necessary to achieve symptomatic relief and a target diameter of 16 mm in a controlled fashion.[106] Expert opinion suggests that perforation risk likely depends more on the change in esophageal diameter in any 1 session rather than absolute dilator size.

14. Effective management of esophageal inflammation in patients with EoE and dysphagia attenuates the need for future endoscopic dilation. It is well accepted that active esophageal eosinophilic infiltration in EoE can lead to esophageal fibrosis and stenosis[3,107] and that 50% of EoE patients will have recurrent dysphagia at 15 months after dilation if not treated with maintenance anti-inflammatory therapy.[66] These data suggest that control of esophageal inflammation reduces the need for dilation. Specifically, 2 studies examined the effect of steroid therapy on the need for recurrent esophageal dilation after an initial dilation or series of dilations. Runge et al[108] found that patients with a histologic response to steroids (defined as a peak esophageal eosinophil count <15 eos/hpf) had a 65% decrease in the need for subsequent dilation after 19 months. Additionally, half as many dilations were required to achieve a similar increase in esophageal diameter, as compared with nonhistologic responders to steroids. This finding suggests that control of inflammation may not only lead to fewer dilations over time but may be associated with a greater response to initial dilation. Schupack et al[109] studied the effect of maintenance therapy on the need for recurrent dilation. Recurrent dilation was needed in 29% of those placed on maintenance therapy compared with 89% of those not on maintenance therapy over a 3-year follow-up (hazard ratio, .12; $P < .001$). Of note, 75% of the maintenance therapy group requiring repeat dilation for symptoms had either stopped therapy or lost response to maintenance therapy and were not in histologic remission at the time of the repeat dilation. In a third study that examined adult EoE patients with strictures <10 mm diameter, histologic remission (<15 eos/hpf) was significantly associated with successfully achieving a diameter ≥15 mm with dilations.[94] It remains unclear if the ability of medical therapy to reduce dilations is mediated by reversal of esophageal fibrosis or inflammation.

15. In patients with EoE, different dilation techniques chosen on the basis of stricture characteristics and endoscopist preference are acceptable for performing dilation therapy. Endoscopy with biopsy sampling accurately identifies the inflammation associated with EoE but often misses esophageal narrowing in the range of 12 to 15 mm.[110] Studies at the Mayo Clinic found that endoscopy had poor sensitivity (14.7%) and only modest specificity (79.2%) for identifying esophageal

strictures when compared with a barium esophagram.[110] Similar findings have been shown in children.[111] Even at a cutoff diameter of <15 mm, endoscopy had a sensitivity of only 25% for the diffusely narrowed esophagus and more difficult-to-identify proximal strictures. Thus, the endoscopist must assiduously evaluate the esophagus for obvious strictures in multiple sites at the time of endoscopy, particularly if a nondominant symptomatic stricture requiring dilation alone is not seen. If nonvisualized symptomatic strictures are suspected, careful empiric panesophageal dilation should be considered with the goal of getting to an esophageal lumen of at least 16 mm. This can be accomplished with any of the dilation techniques. By "starting low and going slow" and progressing gradually to this lumen size, procedures are performed safely and yield symptomatic benefit.[106,112]

In the context of dilating the esophagus, the literature suggests equal efficacy with bougies or through-the-scope balloons.[95,96] Bougie dilation reliably dilates to a fixed diameter, is rapidly performed, is inexpensive, and dilates the entire esophagus to the chosen diameter. Savary bougies over a guidewire are preferred for more narrowed strictures (<15 mm). Fluoroscopy is rarely needed when both adult and 5-mm pediatric endoscopes are available. The Maloney bougies may be used for larger-diameter dilations and give excellent tactile sensation of lumen resistance. Dilation should be stopped if moderate resistance is encountered or repeat endoscopy shows mucosal disruption.[104]

Through-the-scope balloon dilation can be adapted for panesophageal dilation by using a pull-through technique.[113] After examining the entire esophagus, a multisize 8-9-10-mm balloon is positioned across the esophagogastric junction if there is resistance to passage of an adult endoscope or a 10-11-12-mm balloon if the endoscope passes easily. The balloon is inflated to the smallest diameter, positioned in front of the endoscope, and slowly withdrawn from distal to proximal until the entire esophagus is examined. Lumen narrowing is appreciated by the inability to easily pull the balloon through the region. If no resistance occurs, the procedure is repeated with the next size balloon in a serial fashion in a search for subtle strictures. The procedure is terminated when a mucosal tear can be seen through the transparent balloon. The initial balloon size may need to be modified in the presence of strictures narrower than 8-mm diameter. A recently published study on 50 prospectively included adults with EoE found the BougieCap (Ovesco), a single-use, dome-shaped, transparent, hard-plastic cap that is attached to the tip of the endoscope using circular tape, is technically feasible and safe and may offer significant short-term symptomatic improvement.[101]

16. In patients with fibrostenosing EoE, dilation therapy should occur in conjunction with effective medical or diet elimination therapy for management of dysphagia. Fibrostenosing disease and narrow-caliber esophagus, defined as the inability to pass a standard-caliber adult endoscope, are among the most severe adverse events of EoE. Although dilation alone without concomitant medical therapy may provide symptom relief for up to 15 months, this therapeutic approach does not ameliorate underlying esophageal eosinophilia and ongoing remodeling.[66] Several lines of evidence suggest that achieving histologic remission enhances both short- and long-term success of esophageal dilation at reducing symptoms. A single-center cohort study of 55 patients who underwent initial esophageal dilation followed by topical steroid therapy found that histologic responders, defined by <15 eos/hpf, required fewer subsequent dilations than nonresponders (1.6 vs 4.6, $P = .03$).[108] Despite undergoing significantly fewer dilations per patient, responders achieved a similar increase in esophageal diameter with dilation compared with nonresponders from the first to the last recorded procedure. Control of inflammation with topical steroids was associated with a 65% decrease in the number of subsequent dilations to maintain the same esophageal caliber. Subsequently, a single-center case series of 66 EoE patients with an esophageal diameter ≤10 mm at 1 point in their disease were treated with repeated dilation in conjunction with medical or dietary therapy to determine which variables were associated with endoscopic response defined by an improvement in esophageal diameter to 13 mm and to 15 mm.[93] Initial esophageal diameter (odds ratio, 1.58; 95% CI, 1.06-2.35; $P = .025$) and histologic remission (odds ratio, 34.97; 95% CI, 6.45-189.49; $P < .0001$) were significantly associated with achieving a diameter ≥15 mm. Further supportive evidence comes from a cohort study from the Mayo Clinic in which the need for repeat dilation in EoE patients after an initial dilation was lower in patients on maintenance therapy, and most of those on medical treatment that required repeat dilation were not in histologic remission at the time of repeat dilation.[109]

Cessation of medical therapy after achievement of histologic remission (<15 eos/hpf) may also have implications. A 1-year observational study after cessation of therapy in 58 subjects in a randomized clinical trial of budesonide versus fluticasone found that in patients with baseline strictures, esophageal caliber decreased during the observation phase (14.8 ± 2.8 vs 13.7 ± 3.5 mm, $P < .001$).[114] Despite achieving a dilation size of 16.7 ± 1.7 mm at the time of histologic response and entry into observation, a size of only 15.4 ± 2.3 mm was found at the time of symptom recurrence while off treatment ($P = .003$). Further indirect evidence for the value of control of inflammation comes from a phase II study of dupilumab, a monoclonal antibody to the common interleukin-4/13 receptor alpha chain, which suggests that adequate control of inflammation may also improve esophageal distensibility and therefore lessen the need for dilation.[59] Current evidence supports achieving and maintaining

histologic remission to enhance the effectiveness of esophageal dilation and attenuate the need for repeat dilation.[69]

17. In patients with fibrostenosing EoE with inflammatory activity, dilation can be done safely. The early literature on EoE raised concerns regarding the safety of dilation of EoE strictures because of apparent fragility of the esophageal mucosa and development of deep tears after dilation or even passage of the upper endoscope.[115] In particular, several case reports and case series presented serious adverse events associated with dilation, including perforation and clinically significant hemorrhage,[116,117] and may have led to some hesitancy in performing dilation in symptomatic EoE patients with active inflammation or in those not on treatment. More recent larger studies have demonstrated that dilation in EoE is safe, with an adverse event rate similar to dilation of other benign esophageal strictures.[4,6] The type of dilator used (bougie or balloon) does not appear to influence risk.[118]

Several systematic reviews have explored the safety of endoscopic dilation in EoE patients, and all have demonstrated that the rate of serious adverse events is very low.[95-97,119] In 1 limited meta-analysis, major adverse events occurred in <1% of EoE patients undergoing dilation.[119] More recent larger systematic reviews have been published that include data from both pediatric and adult patients and that have very similar adverse event rates.[95-97] Among 845 EoE patients who underwent a total of 1820 dilations, perforations were found to occur in .38%, hemorrhage in .05%, and hospitalizations in .67%. No deaths were reported after dilation.[95] In another systematic review that included 1607 EoE patients, 809 had dilation with similarly low adverse event rates of perforation in .81%, hemorrhage in .38%, and hospitalization in .74%.[97] In a third study of 977 EoE patients who underwent a total of 2034 dilations, perforations occurred in .033%, clinically significant hemorrhage in .028%, and hospitalization in .689%. Across all 3 studies, most perforations were reported before 2009.[96]

Small studies have suggested that predictive factors of postdilation adverse events in EoE may include younger age, repeat dilations, and the presence of a proximal stricture; however, these findings differ from those of larger studies and did not include active inflammation as a potential risk factor.[4,120] Specifically, none of these case series or meta-analyses controlled analyses for patients with effectively treated mucosal eosinophilia and rather examined the safety of dilation in a mixed EoE population that included patients with active disease. In 1 study, topical steroids were used in 58% (range, 6%-100% [15 studies]), followed by proton pump inhibitors in 56% (range, 12%-100% [16 studies]) and diet (mean, 12%; range, 0%-23% [8 studies]), but histologic remission was not assessed.[95] Through their consensus process, the working group has agreed that diverse and extensive published experience supports the use of dilation in EoE patients in the presence of indicated criteria, regardless of whether they have inflammatory disease activity or are not on EoE treatment.

18. Empiric dilation may be performed for persistent dysphagia in the presence of a normal-appearing esophageal diameter by endoscopy and histologic remission achieved with medical or dietary therapy. Esophageal dilation is effective at improving symptoms of dysphagia in patients with EoE, especially in those patients with esophageal strictures or a narrow-caliber esophagus.[71,95] Although dilation treats 1 of the sequelae of EoE (ie, fibrosis/narrowing), it is not effective at treating the underlying cause of the disease (ie, eosinophilic-predominant esophageal inflammation).[65] EoE leads to subepithelial fibrous remodeling,[121] which perturbs esophageal function and leads to dysmotility,[122] esophageal rigidity,[123] and dysphagia. Even when patients may have achieved endoscopic and histologic remission of their disease, longstanding inflammation can result in irreversible structural changes within the esophagus.[124] This is particularly problematic when a tight stricture and/or small-caliber esophagus are present. Consequently, given that dysphagia may persist despite adequate medical therapy and that esophageal dilation can be safely performed to improve symptoms in the short term,[71] it is appropriate to consider dilation for extant visualized strictures or empirically when a stricture is not seen endoscopically. Importantly, the probability and frequency of requiring esophageal dilation is significantly decreased in patients with histologic remission; thus, optimizing medical therapy in patients with EoE is essential.[108] When stricture-directed or empiric dilation is performed, the same considerations for careful selection of initial dilator size and assessment of luminal caliber, as discussed above, still hold.

19. Most EoE patients with radiographically or endoscopically demonstrated perforation will respond to conservative therapy; endoscopic and surgical interventions are rarely needed. Esophageal perforation in the setting of EoE is uncommon.[125] It can occur in patients with previously undiagnosed EoE because of prolonged food impaction associated with Boerhaave syndrome or after endoscopic instrumentation.[125-127] Endoscopic causes of perforation include attempting to advance an impacted food bolus, which is a more common cause of perforation than after esophageal dilation alone.[126]

Management of esophageal perforation in the setting of EoE is similar to management of perforation in the absence of EoE[128] and is nonsurgical in most cases. If recognized early, management of small perforations consists of keeping the patient NPO (nothing per mouth) and administering antibiotics to cover oral flora. Clip

placement for closure, either through-the-scope or over-the-scope, can be attempted but is often not technically successful in the setting of EoE because of the presence of underlying fibrosis. Short-duration placement (≤4 weeks) of a covered self-expandable esophageal stent to seal the perforation is an option,[126] particularly when larger perforations are present. Because most commercially available stents can be oversized in diameter in relation to a small-caliber esophagus, their use can lead to excessive patient discomfort. Therefore, a smaller available diameter stent, which is usually 18 mm in the mid-body with outer flanges that are often 5 mm larger in diameter, is recommended. Fully covered stents that have bare ends that embed into the esophagus are preferable because of their ease of removal but are more likely to migrate than partially covered stents.

When fluid and debris pass outside the esophageal lumen through the perforation, surgical management and/or tube-assisted drainage through the perforation and/or in the pleural cavity is often required.[128] Contamination may occur at the time of attempted food disimpaction, when presentation is delayed, and/or the perforation is unrecognized. Finally, when managing esophageal perforations in EoE, as in any perforation, time is of the essence. Treatment at the time of or soon after perforation, particularly within the first 24 hours, increases the chance of response to less-complicated therapy. In 1 study of esophageal perforation from non-EoE causes, the reported mortality from treated esophageal perforation was 10% to 25% when therapy was initiated within 24 hours of perforation but rose to 40% to 60% when the treatment was delayed beyond 48 hours.[129] In contrast, death from perforation in a patient with EoE has not been reported.

Monitoring disease

20. In patients with EoE in remission, continued monitoring with symptoms should be performed. Consideration should be given to periodic endoscopy and biopsy sampling. Because EoE is a chronic and progressive disease that cannot be cured, monitoring patients after initial diagnosis is necessary.[3,130,131] Several studies clearly demonstrated that symptoms and inflammation recur consistently after cessation of successful medical or dietary therapy.[79,132] Further, it is well known that inflammatory activity and symptom severity have only a modest correlation.[81] These disease-inherent features have several practical consequences. First, once diagnosed, EoE requires a long-term management strategy. Second, anti-inflammatory maintenance treatment must be continued after achieving a state of remission. Third, patients with ongoing treatment need to have regularly scheduled clinical appointments to assess for disease-related adverse events and for side effects of the drugs or diets. Fourth, because absence of symptoms is not a guarantee of endoscopic or histologic remission, a periodic assessment of inflammatory activity using endoscopy with structured biopsy sampling or with less-invasive methods such as the string or sponge test[133,134] can be considered in symptom-free patients. There are little data to guide the frequency of clinical and endoscopic assessments, although expert opinion dictates that at least an annual clinical evaluation in well-controlled patients is reasonable.

DISCUSSION

The diagnosis and management of EoE is based largely on performing endoscopy, which currently represents the only well-accepted means of assessing the severity of typical endoscopic features, procuring esophageal tissue for histologic analysis, and dilating esophageal strictures. Although less-invasive tools are being evaluated as alternatives to endoscopy for EoE, they have yet to be studied prospectively or in randomized controlled trials. Similarly, there have been no randomized controlled studies that compare outcomes of endoscopy-guided versus empiric medical therapy for EoE.

The Delphi process is a well-established iterative approach to achieving consensus across subject experts in the absence of uniformly high-quality data necessary to develop a purely evidenced-based guideline.[135-137] As used for our purposes here, the Delphi process generally involves a series of "rounds," where a leader summarizes the discussion between each round without identifying specific discussants' comments. Between rounds, participants individually and as a group revise the statements based on the discussion. At the conclusion of the process, the group generates an accepted list of statements by virtue of discussion and voting.

The Delphi process that generated this document on the use of endoscopy in EoE is timely. Both the incidence and prevalence of EoE have increased significantly on the global stage since its original description. This is in contrast to EoE being viewed and classified by the National Institutes of Health as a rare disease. For example, in Denmark, the incidence has increased 10-fold,[138] whereas the estimated prevalence of EoE in the Western world is 1 in 2500 individuals.[139] In more-recent population-based studies carried out with current EoE diagnostic criteria, the pooled prevalence of EoE globally is 63.2 cases per 100,000, or about 1 in 1500 inhabitants.[140] The increase in prevalence and incidence of EoE is also contributing to a rising healthcare cost burden of which much, if not most, is driven by the performance of endoscopy with biopsy sampling and dilation.[141] One recent cost analysis found the rate and mean costs of hospital admissions for EoE are markedly increased in the United States at a rate that was 10-fold higher than inflation from 2010 to 2016.[142]

This Delphi process included both adult and pediatric gastroenterologists and resulted in 20 consensus statements for guiding endoscopic practice in the care of patients with EoE along 3 broad areas: use of endoscopy in diagnosis, prediction of disease course, and treatment of

EoE. In addition, we anticipate that the recommendations may also be helpful for nongastroenterologists, including allergists, internists, and pediatricians, involved in the care of patients with EoE. As often occurs in clinical practice guideline development, the content of these statements may appear intuitive and repetitive. For example, endoscopic dilation can be considered in all patients with EoE and an esophageal stricture with dysphagia. Similarly, 3 statements support using dilation before and after achieving and maintaining mucosal healing. These statements were all considered and ultimately achieved consensus through the voting process. Collectively, they reinforce the role of dilation in all aspects of dysphagia and stricturing disease occurring with EoE.

Further, as fundamental to the Delphi process, we also considered statements that could not be modified and accepted and yet may also deserve discussion. For example, periodic dilation therapy may be adequate for treating symptoms of EoE in patients with fibrostenosis without the use of pharmacologic or diet therapy and have even been shown to demonstrate remission of dysphagia for as long as 15 months.[66] The group considered that such a strategy may have safety benefits both in terms of immediate procedural safety and elimination of the need for long-term proton pump inhibitor or topical steroid use, which may also incur risk. The group also considered the evidence that absence of medical therapy may be associated with esophageal fibrosis and stricture formation. Similarly, the statement that all esophageal biopsy specimens should be placed into 1 jar (rather than into 2 jars separating proximal/mid- and distal esophagus) was not approved. Data demonstrate histologic detection with biopsy sampling of the distal esophagus is 100% sensitive. As a result, the finding of esophageal eosinophilia in the distal esophagus is not helpful in differentiating EoE from GERD-induced esophageal eosinophilia.[21,24] Further, isolated proximal/mid-esophageal eosinophilia does not occur in the absence of distal esophageal eosinophilia and its presence is not a reliable indicator of EoE as the cause. From a whole-organ viewpoint, the gross changes in esophageal appearance as graded on EREFS are not known to selectively involve the proximal and/or mid-esophagus without the distal esophagus. These are all reasons not to incur the increased expense of processing and interpreting biopsy samples from 2 esophageal locations. Nevertheless, most experts believe there is merit at this time to biopsy sample both the mid-/proximal esophagus, and some experts endorse the use of separate biopsy jars by esophageal location. Whether further data will allow more assured answers to the unapproved statements remains unclear. A proposal to define specific EREFS scores for remission and relapse also arose. Although this would better guide clinical use of the score, data are only beginning to emerge on this question.

This Delphi process for EoE management has several limitations. For example, the coronavirus disease 2019 crisis mandated that discussion and voting occurred using a virtual platform. Whether the quality of discussion through this process was as robust as a face-to-face meeting is unclear; however, we believed that we had detailed discussions with engaged participants. Another limitation is the marked lack of high-quality evidence-based data, or in some areas lack of any data, to evaluate the proposed statements. For example, no data are available to assess if biopsy samples taken for EoE at the time of rather than after initial presentation of EoE with food impaction rather than at subsequent endoscopy alters the patient's course of EoE. As a result, much of the consensus is based on good clinical judgment by the experts with data from published studies. On the other hand, several strengths were apparent to this process. EoE experts were chosen from multiple fields where EoE care is administered to avoid the bias of a primarily endoscopy-focused group. Although the online discussion may appear to be a limitation, in fact, it led to broad solicitation of opinion from all members of the committee in composing statements. We also performed a 2-step process where a core committee vetted statements first, followed by an approval by a vetting group in composing the final list.

In conclusion, this Delphi consensus conference proposed 20 statements for the use of endoscopy in the diagnosis, prognostication, and treatment of EoE with the goal of providing clinical guidance to providers caring for EoE patients. In combination with proposed statements that could not be approved at this time, it is the working committee's hope that future studies will not only provide further support for approved statements but more clarification on other important questions around the role of endoscopy in EoE.

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Abbreviations: EGID, eosinophilic GI disorder; EoE, eosinophilic esophagitis; eos/hpf, eosinophils per high-power field; EREFS, Endoscopic Reference System.

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*Member of the initial core group of experts.

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SUPPLEMENTARY TABLE 1. Eosinophilic esophagitis panel member experts

Name	Institution	Specialty
Aceves, S*	University of California San Diego and Rady Children's Hospital	Pediatric allergy
Alexander, J	Mayo Clinic	Gastroenterology
Baron, T*	University of North Carolina School of Medicine	Gastroenterology
Bredenoord, A	Academic Medical Center, Amsterdam	Gastroenterology
Day, LJ*	University of California San Francisco	Gastroenterology
Dellon, ES*	University of North Carolina School of Medicine	Gastroenterology and esophagology
Falk, G	University of Pennsylvania Health System	Gastroenterology
Furuta, GT	University of Colorado School of Medicine; Children's Hospital Colorado	Pediatric gastroenterology
Gonsalves, N	Northwestern University Feinberg School of Medicine	Gastroenterology
Hirano, I*	Northwestern University Feinberg School of Medicine	Gastroenterology
Konda, V*	Baylor University Medical Center	Gastroenterology
Lucendo, AJ	Hospital General de Tomelloso; Instituto de Investigación Sanitaria Princesa (IIS-IP) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD)	Gastroenterology
Moawad, F	Scripps Health Uniformed Services	Gastroenterology
Petersen, K*	University of Utah Health	Gastroenterology
Putnam, P	Cincinnati Children's Hospital Medical Center	Pediatric gastroenterology
Richter, J	University of South Florida Health	Gastroenterology
Schoepfer, A	Centre Hospitalier Universitaire Vaudois and University of Lausanne	Gastroenterology
Straumann, A	Facharzt FMH fur Gastroenterologie u. Innere Medizin	Gastroenterology

*Member of the initial core group.

SUPPLEMENTARY TABLE 2. Statements that did not achieve consensus

1. At index endoscopy for EoE patients, multiple biopsy samples should be taken from the stomach and duodenum to assess for eosinophilic gastroenteritis in patients without compatible symptoms and/or endoscopic abnormalities.
2. In patients with EoE, an EREFS score $\leq$2 (as measured for the most involved areas throughout the esophagus on a scale from 0 to 9, with edema 0/1, rings 0/1/2/3, exudates 0/1/2, furrows 0/1/2, and stricture 0/1, is an adequate definition of remission.
3. In patients with EoE, an EREFS score >3 is considered evidence of relapse.
4. In patients with EoE, baseline impedance planimetry should be performed during endoscopy.
5. Using the sponge or string device is sufficient to monitor response to therapy in EoE.
6. In patients with EoE, esophageal stenting may be performed to treat iatrogenic or spontaneous perforation because of eosinophilic esophagitis.
7. All esophageal biopsy samples should be placed into 1 jar.
8. Periodic dilation therapy is inadequate for treating symptoms of EoE in patients with esophageal fibrostenosis without the use of effective pharmacologic or diet therapy.

EoE, Eosinophilic esophagitis; *EREFS*, Endoscopic Reference System.