Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/gi-insights/applying-the-2020-eosinophilic-esophagitis-guidelines-to-practice/12624/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Applying the 2020 Eosinophilic Esophagitis Guidelines to Practice

Dr. Nandi:
It's 2 AM when you get the call from the ER. Of course, it's an esophageal food impaction. Earlier that evening, a 19-year-old young adult has enjoyed some filet mignon but now was reporting dysphasia, chest pressure, and difficulty swallowing their secretions. You must go in. You assemble your A-Team, and descend upon the OR, and just as you expected, you observe esophageal ringing, longitudinal furrows with an obstructive meat bolus. After removing the bolus, taking biopsies, and saving the day, you follow up with the patient as an outpatient in clinic and relay a formal diagnosis of eosinophilic esophagitis.

Your patient ponders this for a minute and then, calm and collected, turns to you and asks, "So what's next doc? That was an alarming experience. How can I prevent this from happening again?" That's where Dr. Kristle Lynch comes to the rescue. She will be reviewing highlights on the latest AGA EoE guidelines published this past 2020 and help teach us how to best manage our EoE patients for the long term. Dr. Kristle Lynch is an Associate Professor of Medicine in the Division of Gastroenterology and Hepatology at the Perelman School of Medicine at the University of Pennsylvania. She is an esophagologist extraordinaire with clinical specialties that not only encompass esophageal dysmotility, EoE, achalasia, and esophagogastric junction outflow obstruction, but all things esophagus. Dr. Lynch, welcome to *GI Insights*.

Dr. Lynch:
Thank you. It's a pleasure to be here. And thank you for that riveting introduction.

Dr. Nandi:
You're quite welcome. And we really are excited to have you here. You know, EoE is one of these challenging disease entities to manage for many patients. And we see this both in our pediatric and adult populations. With treatment regimens consisting of PPIs, steroids, and elimination diets, the management can still be challenging, and so I'm really happy that AGA was able to release these EoE guidelines in 2020 because they're impactful and provide good strategies. Now what do you see as the most significant changes in these 2020 guidelines?

Dr. Lynch:
So yeah, the AGA Joint Task Force when they published these updated guidelines in 2020, there are a few important points to highlight. But one thing I will mention that stands out is a reminder that the term PPI-responsive esophageal eosinophilia is no longer used. So currently after exclusion of secondary causes of esophageal eosinophils, symptomatic esophageal eosinophilia, is now termed EoE. PPIs are an effective primary therapeutic option for EoE, but response to PPI no longer defines a distinct entity. And this was based on numerous studies showing that patients with EoE and what was previously coined PPI-RE or PPI-responsive esophageal eosinophilia shared many characteristics. I mean, demographics, clinical presentation, endoscopic findings, type of immune response, and even EoE transcriptome panel. So I think it's definitely important to keep in mind that while PPIs are a great primary therapeutic option for EoE, they do not define a distinct entity.

Dr. Nandi:
So I think that's really insightful that there is some evolving thought on how we coin and how we term or label these eosinophilic patients, especially in response to PPIs. Looking through the recommendations, I noted that many of the studies are not necessarily as well powered due to this being a rare disease entity. But many of the recommendations are rated conditional. That said, one of the most important recommendations I thought was that we should be providing our patients more topical inhaled steroids as opposed to systemic corticosteroids like prednisone. But how should clinicians really apply to this to their patients? How long should the patient be on a topical inhaled corticosteroid? Is it safe?

Dr. Lynch:
This is a great question. So we never use systemic steroids in EoE patients. There have been numerous studies showing us that topical steroids are successful in treating patients. But as you said, Neil, due to the rarity of this disease, the numbers aren't as robust as one might hope. However, there were eight double blind placebo-controlled studies about the over 400 patients, and these looked at topical steroids versus placebo. The pooled response rate was 65% in patients on steroids versus 15% of patients on placebo. And so this was significant.

One thing to note about these studies is that these were largely patients who had failed PPI. This was intuitively from the PPI-RE controversy that I previously mentioned. And so steroids are definitely successful in patients.

Now the question as to whether a patient should be left indefinitely on these steroids can be tricky. So we know that long-term therapy is critical for EoE. We can't just do a dilation, remove that food, and tell the patient to go on a PPI for eight weeks or to do fluticasones inhaler swallowed for eight weeks. There are many studies showing us that when therapy is stopped in patients in remission, there is recurrence of disease.

So for example, there was one study where 100% of patients were in deep remission, meaning endoscopic, histologic, and symptomatic remission, and they stopped their steroids. And 82% of patients had clinical relapse off of therapy at a median of 22 weeks. And though patients don't need to necessarily be on steroids long term, they need to be on something long term. A lot of our patients are young, and I've had patients on steroids, they call me five years later, they're ready to try the diet. Or they're on the diet, they're sick of the diet a couple years later, they want to go on steroids. I think that is realistic for the future of EoE, that patients may not always be on the same consistent therapy. And also with evolving new therapies, I could see things changing, but it's really important that patients are on something long term because this is a chronic disease.

Dr. Nandi:
I think you hit some really important points there. And speaking as one IBDologist to an esophagologist, in our world of IBD, we talk a lot about goals of therapy, treat-to-target and endoscopic remission, what are the goals of therapy for an EoE patient that we should have in the short term in the long term?

Dr. Lynch:
So currently, our studies are limited to the main primary endpoint being histologic remission, so less than 15 eosinophils per high-power fields. And that has many advantages. It is well defined, it is clear cut, you take the biopsies and it's a routine thing for pathologists to do. However, that doesn't really encompass the patient as a whole regarding endoscopic findings, so the EREFS and the symptoms. So EREFS, briefly, being the classic endoscopic findings that we grade on every endoscopy in patients with EoE. So E, the first E for edema, R for rings, E for exudates, F for furrows, and S for strictures.

It also doesn't take into account the patient's symptoms and if the symptoms have improved with this therapy. We know from prior studies that symptoms do not always correspond with histologic findings. And that's why we even do endoscopy is to check if patients are in remission. Otherwise, we certainly wouldn't put the patient through that.

And so I think the future of EoE has more of a spectrum of histologic improvement or remission, endoscopic improvement or remission, and symptomatic improvement or remission. And that's something that we're looking towards. But currently with prior studies, the primary endpoint has typically simply been histologic.

Dr. Nandi:
So that's good that we have to understand where do we apply inhaled corticosteroids and that prednisone is really not an established therapy for EoE? What are the long-term safety or adverse event profile of topical inhaled corticosteroids?

Dr. Lynch:
Regarding adverse effects, there are understandably many concerns. So I would logically be concerned for adrenal suppression, fungal infections, potentially local viral infections. There have been rare reports of bone density issues, glucose intolerance, and even cataract formation. Currently, I will say the short-term studies we have showed no significant increased risk of adverse effects as compared with placebo. However, long-term studies looking at side effects are currently ongoing. One thing we should consider here is asthma. For an example, patients with asthma have used topical steroids for therapy for years and this is actually considered a primary routine therapy and their inhalers are considered quite safe. And so we hope to have more data on long-term effects down the road. But I'm optimistic about the outcomes of these studies.

Dr. Nandi:
So this is beautiful, just the way you said that, and then there's a lot of parallels throughout medicine, especially in the GI space. We want patients to look as good on the inside as they feel on the outside, and to scopic remission, histologic remission being very

important endpoints.

For those just tuning in, you're listening to *GI Insights* on ReachMD, and I've been speaking with Dr. Kristle Lynch on her insights and application of the latest AGA eosinophilic esophagitis guidelines published this past 2020.

Now Dr. Lynch, we were just talking about the endpoints of care and what we should really desire to achieve for our patients. I know that PPIs in some studies have demonstrated up to 40% histologic remission, as you said, eosinophils below 15 per high-power field. But it's a multi-pronged approach, as you alluded to, right? It's not necessarily just about PPIs, or just steroids. One of those approaches is dietary. Can you tell us what is your take on the pros and cons and how you apply elimination diets versus some of the elemental diets that we've seen some of our pediatric patients benefit from?

Dr. Lynch:
So regarding elemental diets, these are very successful in achieving histologic remission. However, when you look at studies, most of the study patients were pediatric. There's a limited data in adults. And as you can imagine, there are many barriers to adults using the elemental diet. With children, you have someone monitoring everything that they're eating, but with an adult, it is difficult to be social. It's an expensive diet. And the most commonly used elimination diet in adults is actually the six-food elimination diet over the elemental diet.

So the six-food elimination diet empirically eliminates the six most common food allergen groups. So that'll be wheat and gluten, soy, eggs, dairy, milk, nuts, which is tree nuts and peanuts, and seafood and shellfish. So we consider it six, some people consider that technically eight. And patients will go on this elimination diet for six weeks. This will be followed by an endoscopy to assess if the patient is in histologic remission. If the patient is in histologic remission, we add food groups back in and test them one or two at a time via endoscopy. And the reason we do this is because symptoms do not always correlate with histologic remission. But as you can imagine, this is a long process, with many variants on the diet. It's time consuming, it's expensive, and it requires multiple days off work to come in for these endoscopies. However, at the end of this process, patients have a medication-free method for long-term remission of their disease, which is beautiful. I find that patients really gravitate towards diet or medication. And so it takes a certain type of patient with resources and motivation to do the six-food elimination diet.

There are also variants of the six-food elimination diet. So various other elimination diets include four-food, three-food, two-food, or one-food elimination diet with decreasing success in studies as you go down. There's also been described the 2-4-6 step-up diet. That has been more recently described, but it first eliminates milk and gluten for six weeks. And then non-responders are offered a four-food elimination diet. So they would increasingly avoid eggs and legumes. And then non-responders to this are offered the full six-food elimination diet.

So as you can imagine, this step-up diet may allow us to identify patients before they have to get to the full six-food elimination diet. However, some patients may eventually get there, and it took longer to get there, the process would be longer. So there are definitely pluses and minuses of this.

Dr. Nandi:
Absolutely. And it's very challenging and frustrating for our patients to go through it. But if done in a systematic way, as you said, we can really define the right type of dietary approach to help these patients achieve that histologic and endoscopic remission to avoid fibrosis and scarring. One of the things that sometimes patients bring to the office, which is very frustrating to see, is a food allergy report. Can you comment? What is the utility or role of a food allergy test?

Dr. Lynch:
So the guidelines recommend that an allergy-guided diet is done over no therapy. But unfortunately, studies are showing us that the allergy-guided diet is not as successful as the six-food elimination diet and other variants of the food elimination diet or the elemental diet. So in my clinical practice, we do not routinely use the allergy-guided diet. But some patients come to us on it and there are a handful of patients who are successful on the allergy-guided diet.

Dr. Nandi:
That's good to know what your clinical experience has been and what the guidelines say. In my own practice, I have not found it very useful. I find there's a lot more questions and ambiguity to some of the results. But it's important to know that it works for some but not all. And I think we just need to do more research before we settle on that as an approach to guide our patients.

Now EoE shares a lot of overlapping features with other atopic illnesses such as asthma, eczema, allergic rhinitis, and it's been theorized that some of the immune pathways can be exploited by some common drugs to all these illnesses. Montelukast, cromolyn, TNF therapies and even other cytokine interventions. What's your quick take or what's the latest update on where are we at with these emerging therapies? Are they ready for primetime?

Dr. Lynch:
This is a really exciting area right now. The future of EoE is broad and wide. There are many emerging therapies. So IL-5 is one of the targets being the pro-inflammatory cytokine that finds eosinophils and promotes the eosinophilic trafficking to the esophagus. So benralizumab, which is an IL-5 R alpha receptor antibody, has been approved for use in eosinophilic asthma. So ongoing clinical trials for EoE. Other overlap medication with other atopic illnesses, dupilumab, the IL-4 and IL-13 monoclonal antibody, is currently used for atopic dermatitis and it is shown to be superior to placebo in Phase 2 EoE studies. Further data is currently pending.

Dr. Nandi:
So that seems exciting for sure that we're having so many therapies coming up through the ranks.

Dr. Lynch, I want to thank you so much for your time and joining us on this program. We've learned a lot, and I think we've hit a lot of important highlights for our listeners to be drawn attention to. But Dr. Lynch, thank you so much for joining us today. We really appreciate your time.

Dr. Lynch:
Thank you so much for having me. This is wonderful.

Dr. Nandi:
To access this episode and others from *GI Insights*, please visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. I'm Dr. Neil Nandi. Have a great day and thanks for listening.