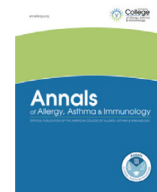




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New diagnostic criteria for eosinophilic esophagitis Will they influence our practice?



It has been quite a journey for the entity known as proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE). The new international consensus diagnostic criteria for eosinophilic esophagitis (EoE), recently published by Dellon et al¹ and summarized by Spergel et al² in this issue, currently state that the diagnosis of EoE can be made if esophageal symptoms and esophageal eosinophilia are present after ruling out other causes of esophageal eosinophilia. An 8- to 12-week trial with a high dose of PPI to rule out PPI-REE, as stated in the 2011 consensus recommendations,³ is no longer considered a requirement to confirm the diagnosis of EoE but rather a therapeutic option for EoE. In other words, the idea that PPI-REE is a separate entity from EoE is vanishing, and patients with PPI-REE are now considered a subset of patients with EoE who respond to PPI, provided other causes of esophageal eosinophilia are ruled out.

This decision to change the diagnostic guidelines was made after a series of studies that showed that (1) patients with PPI-REE and EoE were clinically, endoscopically, and histologically indistinguishable⁴; (2) some adult patients with PPI-REE responded to an EoE-specific diet when they stopped their PPI^{5,6}; (3) PPIs blocked in vitro eotaxin-3 secretion by epithelial cells cultured in an allergic milieu, independent of their anti-acid properties⁷; and (4) EoE and acid-induced gastroesophageal reflux disease (GERD) were not mutually exclusive.⁸

The new consensus diagnostic criteria for EoE will likely influence our clinical practice in several ways. First, our patients previously diagnosed with PPI-REE will be eligible to try other therapies such as dietary restriction therapies and topical corticosteroids (TCSs), 2 commonly used standard-of-care therapies for EoE. However, because all studies using these treatment modalities were performed on patients with PPI-resistant EoE, we do not know the remission rates of diets and TCSs for PPI-responsive patients if they decide to switch therapies, as the consensus summary² points out. Although many patients with PPI-responsive disease might decide to continue PPI therapy in the long term, a large number of families of children with EoE might opt for a dietary trial instead, because diets are typically favored over medications in the pediatric population.

Second, the new guidelines will affect our patients with newly diagnosed EoE when we use the new diagnostic criteria. The consensus summary² states that PPIs are considered good first-line therapy for patients with EoE, given their relatively good safety profile, low cost, convenience of use, and decent success rate compared with other therapies for EoE. However, many patients with newly diag-

nosed EoE might opt for a dietary therapy as a first choice, without recurring first to a PPI. Patients who are generally averse to medication use or those who are concerned about controversial reports concerning the long-term safety of PPIs⁹ would be particularly interested in diet as first-line option. In addition, parents of children with EoE might be very interested in a dietary therapy rather than medications, including PPIs, as experience in pediatric centers specializing in EoE has shown. Therefore, research studies will be needed in the near future to determine the success rate of diets in not only PPI-responsive patients but also PPI-naïve patients. In addition, comparative studies examining the efficacy and safety of long-term PPI vs dietary restrictions and PPI vs TCSs will be needed. In the interim, in our practice, we can offer all available therapy options to patients with PPI-REE and PPI-naïve EoE and clearly explain the lack of knowledge regarding the success rate of these therapies for these particular patients. Careful considerations would have to be made in choosing a therapy option, including the patient's medical history, lifestyle, and potential side effects of each therapy for the particular patient.

Third, one has to be careful not to conclude from the new consensus summary that PPI use in patients with EoE is being eliminated. Recent studies leading to the new diagnostic criteria have shown that EoE and acid-induced GERD are not mutually exclusive. In general, acid-induced GERD is a very prevalent disease in adults and is not uncommon in children. GERD and EoE in a patient can be concurrent and independent or concurrent with one influencing the other.^{2,8} Therefore, a PPI will still have a role as an adjunct therapy for a select number of patients who elect to pursue other therapies for their EoE. Now that PPIs will not have to be tested a priori in our patients, we will likely face a dilemma in those PPI-naïve patients who chose a dietary therapy as first line and do not fully respond. Would we switch their dietary therapy to a high-dose PPI or a TCS or would we add a low-dose PPI as an adjunct therapy knowing that some patients might have concurrent GERD and that a subset of patients with PPI-REE could respond to a lower PPI dose?¹⁰ New studies will be needed to determine which subset of patients with EoE could benefit from a PPI as an adjunct therapy.

In conclusion, the era of PPI use for patients with EoE will not simply disappear with the new consensus diagnostic criteria, but our clinical approach to patients with EoE will change. We urgently need to better understand why some patients with EoE respond to a PPI. We need to confirm in vivo the potential anti-inflammatory effect of the PPI, elucidate other potential mechanisms of action of the PPI in patients with EoE, and study the molecular and genetic determinants of the PPI response. In addition, going forward, clinical trials will need to change their inclusion criteria for patients with EoE, providing justification for any stratification of patients with respect to PPI response. These are exciting times in the field of EoE. After all, EoE is

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still considered a relatively young disease, and its diagnosis and management are considered a work in progress. As a result, one would expect a continuously evolving definition for EoE as more data are generated over the next decade, especially related to its immune and antigen-mediated nature.

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