



Editorial

The asymptomatic patient with eosinophilic esophagitis To treat or not to treat?



Asymptomatic diseases pose therapeutic dilemmas regarding how to balance the benefits and risks of treatment against the long-term complications of untreated disease. In the current issue of the *Annals*, 2 opposing views are presented, highlighting the important aspects of either approach.^{1,2}

Eosinophilic esophagitis (EoE) is a chronic disease,³ with very rare reports of spontaneous remission in the form of histological response to placebo in clinical trials.⁴ Symptoms are intermittent in some patients, and the disease burden is high, affecting physical, emotional, or social domains.⁵ The risk of development of fibrostenotic complications increases with longer disease duration,⁶ although the exact magnitude of this risk remains unknown. This is because, with the exception of early studies with small number of adults, the natural history of EoE has not been studied, and all subsequent studies have been limited by their retrospective design.

No Food and Drug Administration (FDA)-approved EoE therapies are available. Current therapies are not always effective; many have side effects, which can be of physical, emotional, or social nature. Given the absence of FDA-approved therapies, consensus statements have described all commonly used therapies and outlined their efficacy and potential drawbacks, but have not yet provided specific recommendations as to a stepwise approach algorithm for a given patient.³ As a result, when faced with a diagnosis of EoE, a discussion typically occurs between the clinician and patient/caregiver on a therapy choice that is acceptable in the sense that it fulfills the requirement of symptom relief while minimizing the potential for side effects. If the therapy approach is not based on a discussion that balances therapy and its potential side effects against disease symptom severity, the patient ends up not adhering to the therapy and living with the symptoms if tolerable, or requesting a different therapy, or even at times changing providers in the hopes of changing therapy.

One wonders what happens when this balancing act is not needed because the disease is not causing any symptoms. Given that our therapies for EoE are not yet optimized, is it still important to treat? Although Muir et al¹ clearly point out that symptom relief is not the

only indication for therapy, emphasizing that therapy is also important to prevent and treat complications related to esophageal fibrostenosis, Lieberman² counters that the disease is chronic and slowly progressing, rendering longitudinal monitoring a feasible option, with intervention to be made as soon as this complication occurs. Preliminary evidence points to the fact that, indeed, as opposed to other diseases such as asthma, EoE remodeling can potentially be reversed, but more readily so in children.^{7,8} Because esophageal remodeling is a slowly progressive process, early fibrosis might be more likely to reverse than late fibrosis. Conversely, therapies for EoE are often difficult to implement and in many instances not effective; therefore, inducing EoE remission may require more than 1 attempt at treating it, with associated potential for heavy treatment burden and side effects.

Therefore, studies are needed to identify which subset of patients are likely to develop esophageal remodeling, because these patients would be preferentially targeted with therapy early on, even when their symptoms are absent. We also need more clarity as to which dietary restriction therapies are effective through in-depth research of immune mechanisms underlying food-induced pathology in EoE, so that multiple rounds of dietary restrictions to achieve disease control are avoided, as is currently the case.⁹ We also need to await results of the increasing number of drugs being currently tested for EoE, so that we can determine their true efficacy, their optimal method of administration, and a clearer picture of their side effects. Muir et al¹ highlight the risk of fibrostenosis leading to stricture formation that may require periodic esophageal dilatations. We need a better understanding of the patients' perception of these esophageal dilatations. Although physicians consider dilatation a procedure that can and should be avoided, we do not know whether patients view it in the same negative light. Evidence suggests, however, that esophageal remodeling is associated with esophageal dysmotility, which can result in symptoms, even in the absence of a stricture. We definitely need an in-depth evaluation of the effect of esophageal dysmotility in patients with EoE,¹⁰ so that we have a better understanding of the potential harm of esophageal remodeling for each individual patient.

Once known, this balance can then be applied for the asymptomatic patient with EoE, by choosing a therapy that has a reasonable efficacy profile while carrying minimal side effects. Until then, given all the unknowns, when faced with a patient with EoE in the office, a thorough discussion of the pros and cons of treating, including known efficacy rate of each therapy option, potential side effects, and extent of patient and caregiver involvement on the long run with the chosen therapy, need to be discussed with the patient/caregiver. The discussion should take into consideration the importance of the physical, emotional, and social burden of each therapy, when compared with the disease itself. Shared decision making is highly advisable between

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the patient/caregiver and the clinician, ensuring periodic follow-up regardless of the treatment decision.

This brings up a final thought for those of us regularly contributing to relieving the burden of EoE in the lives of children and adults with the disease through research and clinical care. Perhaps it is time that we add another component to our assessment of these patients besides physical symptoms, endoscopic findings, histological findings, and esophageal compliance; and that is quality of life. When addressing any chronic disease, quality of life becomes of paramount importance for patients and their caregivers in deciding whether to treat, which therapy to choose, and even when to “give up.” The asymptomatic EoE patient has the highest burden to bear, given that therapy for EoE is not simple. Choosing a therapy that is not “worse than the disease” on multiple levels including quality of life, following extensive discussion with the patient and family, is key.

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