

# Latest Insights on the Relationship Between Symptoms and Biologic Findings in Adults with Eosinophilic Esophagitis



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## KEYWORDS

- Eosinophilic esophagitis • Patient-reported outcomes • Symptoms • Quality of life
- Regulatory authorities

## KEY POINTS

- Earlier studies had conflicting results on the nature of the relationship between symptoms and biologic findings.
- Based on studies using newly validated PRO measures, the relationship between symptoms and biologic findings in adult patients with EoE is of a nonlinear nature: symptoms tend to be indicative of severe biologic alterations, but lack of symptoms does not exclude presence of mild to moderate biologic alterations.

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- This nonlinear relationship between symptoms and biologic findings has important implications for length of diagnostic delay, selection of the patients for the trials and observational studies, and long-term management of patients with EoE.

**INTRODUCTION**

Eosinophilic esophagitis (EoE) is defined as a chronic, immune/antigen-mediated, esophageal disease, characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation. Adults typically present with swallowing- and nonswallowing-associated pain and dysphagia for solid food that is accompanied by a range of behaviors associated with these symptoms.<sup>1,2</sup> Children, however, experience an array of symptoms, such as vomiting, abdominal pain, and dysphagia, but these seem to vary with age and can be nonspecific.<sup>1,2</sup>

**THE TALE OF TWO STUDIES AND NONLINEAR RELATIONSHIP BETWEEN SYMPTOMS AND BIOLOGIC FINDINGS**

Literature often highlights the controversial relationship between biologic findings and symptoms in adult patients with EoE. For example, Straumann and colleagues<sup>3</sup> have demonstrated in a randomized, placebo-controlled 15-day trial of adult/adolescent patients (36 patients, 18 patients in the experimental group, mean esophageal eosinophil count at baseline of 148 [standard deviation  $\pm$  61] per high-power field [hpf]) that treatment with topical budesonide improved histologic findings and symptoms as assessed by an ad hoc–developed patient-reported outcomes (PROs) instrument designed to assess dysphagia frequency and severity of dysphagia episodes (Straumann Dysphagia Instrument). However, in a randomized, placebo-controlled 6-week trial of 42 adult patients with mean esophageal eosinophil count at baseline of 26 (range, 12–89 per hpf), Alexander and colleagues<sup>4</sup> showed that treatment with topical fluticasone improves the esophageal eosinophilia, but not symptoms as assessed by two items of the Mayo Dysphagia Questionnaire 14-day version (validated but not specifically for EoE PRO instrument).

In light of the current literature, it is absolutely clear that these studies epitomize two pieces of puzzle that, when put together, tell a great deal about “the controversial” relationship between symptoms and biologic findings. However, without the data from larger observational studies (discussed later), patient selection for the studies is found to be somewhat challenging. In fact, researchers grappling with any condition for which no disease-specific validated PRO measures have been developed have faced similar challenges. For example, using the data of a much larger trial that compared three types of treatment (infliximab alone, azathioprine alone, and combined treatment with infliximab and azathioprine in 508 patients), Peyrin-Biroulet and colleagues<sup>5</sup> have shown an apparent “disconnect” between the biologic disease activity as assessed by systemic C-reactive protein, fecal calprotectin levels, and clinical activity as assessed by Crohn’s Disease Activity Index (CDAI). CDAI is a composite measure that includes, among other things, clinician-reported symptoms, laboratory findings, and presence of complications. Authors attributed such disconnect to CDAI properties, namely lack of specificity of included symptoms for the diseases and lack of sensitivity of these symptoms for

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