

and underdeveloped countries, and new or infrequent foods are increasingly being diagnosed as a result of changes in consumption patterns owing to globalization. Seed allergy, specifically flaxseed allergy, should be considered in the differential diagnosis of food allergy.

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## Should children with immunoglobulin E–mediated food allergy be screened for eosinophilic esophagitis?



Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus, involving an allergen-mediated process highly associated with other atopic conditions.<sup>1–3</sup> Several studies have identified the significance of food antigens underlying EoE development, evidenced by treatment using food elimination diets and the emergence of EoE with oral immunotherapy.<sup>4,5</sup> The progression from immunoglobulin E–mediated food allergy (IgE-FA) to EoE has been illustrated, either from the same or different food triggers.<sup>6,7</sup> Still, EoE remains difficult to diagnose because of nonspecific or masking of symptoms, disease underrecognition, and the need for an invasive diagnostic procedure, resulting in diagnostic delay. This contributes to the risk of stricture formation and fibrostenosis.<sup>8</sup> Currently, no interventional studies have evaluated the use of screening for EoE potentially relevant in higher-risk populations such as those with IgE-FA.<sup>7</sup> Thus, we sought to determine the extent to which children with IgE-FA (but without a diagnosis of EoE) reported EoE symptoms through formal screening.

From April to October 2021, we surveyed all children with IgE-FA in our allergy practice using the Pediatric Eosinophilic Esophagitis Symptom Severity Module (PEESS) version 2.0, a validated pediatric-specific questionnaire to assess for symptoms of EoE in children ages 8 to 18 years and parent proxy ages 2 to 18 years.<sup>9</sup> Dysphagia-specific scores were primarily evaluated given the established correlation of these scores with increased EoE activity histologically.<sup>9</sup> In addition,

we included a supplemental question (“do you ever feel food going down after swallowing?”), which was considered a potentially substantial question relevant to EoE on the basis of the authors’ clinical experience. Surveys were administered at routine office visits. Children with previously established EoE and IgE-FA were included for comparative purposes. Patients with EoE but without IgE-FA were excluded. Our primary outcome was a positive response to dysphagia-specific items (items 7–12) on the PEESS, in which patients scored the frequency of symptoms as greater than or equal to “1 or more times a week” or severity as “kind of bad” or greater. A “yes” response to the supplemental questions was a co-primary outcome. Secondary outcomes included positive responses on non-dysphagia-specific PEESS items and the correlation between child and parent responses.

There were 263 families surveyed over a 6-month study period. We excluded 40 charts (4 with EoE but no IgE-FA and 36 incomplete surveys). The remaining 223 (210 with IgE-FA only and 13 with IgE-FA and EoE) were analyzed. The patients’ median age was 9 years (range 2–18) and 64% were boys. The patients were atopic, including 55%, 32%, and 23% with allergic rhinitis, asthma, and atopic dermatitis, respectively. Roughly 10% reported a family history of EoE.

For our primary outcome (Table 1), 26 children (16%) endorsed dysphagia symptoms (13% with IgE-FA only). An additional 25 patients responded affirmatively to our supplemental question, cumulatively equaling 31% of children with symptoms of dysphagia or abnormal feeding sensation, 28% in children with IgE-FA without EoE diagnosis. Positive parent responses were elicited in 22 (12%) overall and 12% in those with IgE-FA only. In total, 51 (24%) participants with IgE-FA without EoE elicited any positive (child or parent) response.

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**Table 1**  
Study Outcomes.

| Outcomes                        | IgE-FA Total   | IgE-FA Only    | IgE-FA and EoE |
|---------------------------------|----------------|----------------|----------------|
| Survey totals, N (%)            | 223 (100)      | 210 (94)       | 13 (6)         |
| Child                           | 166 (74)       | 157 (95)       | 9 (5)          |
| Parent proxy                    | 178 (80)       | 168 (94)       | 10 (6)         |
| Primary outcome, N (%)          |                |                |                |
| Child                           |                |                |                |
| Dysphagia                       | 26 (16)        | 21 (13)        | 5 (55)         |
| Supplemental                    | 34 (20)        | 32 (20)        | 2 (18)         |
| Supplemental only               | 25 (15)        | 24 (15)        | 1 (11)         |
| Parent                          |                |                |                |
| Dysphagia                       | 22 (12)        | 20 (12)        | 2 (20)         |
| Supplemental                    | n/a            | n/a            | n/a            |
| Supplemental only               | n/a            | n/a            | n/a            |
| Secondary outcomes, N (%)       |                |                |                |
| Child                           |                |                |                |
| Dysphagia and other             | 23 (88)        | 19 (90)        | 4 (80)         |
| Supplemental and other          | 13 (52)        | 13 (54)        | 0 (0)          |
| Concordance, N (%) <sup>a</sup> | Child positive | Child negative |                |
| Parent positive                 | 9 (18)         | 11 (23)        |                |
| Parent negative                 | 12 (25)        | n/a            |                |

Abbreviations: EoE, eosinophilic esophagitis; IgE-FA, immunoglobulin E-mediated food allergy.

<sup>a</sup>Percent of all positive dysphagia responses.

Of the patients with IgE-FA meeting the primary end point for dysphagia, 19 (90%) also reported positive responses to a nondysphagia item. Similarly, more than half (13 of 24) of patients who had a positive response only to the supplemental question reported at least 1 positive response to a nondysphagia PEESS item. Concordance between child and parent surveys was low, with only 9 consistent positive dysphagia responses. Furthermore, a negative parent response was elicited in 12 of 21 (57%) cases in which children (IgE-FA only) reported dysphagia.

In this 6-month pilot study, we identified a relatively high proportion of children (nearly 30%) and parental surveys (12%) with IgE-FA (but without EoE) who endorsed symptoms of dysphagia or abnormal feeding sensation, raising significant concern for potential undiagnosed EoE. Comparatively, the rate of dysphagia identified is similar to the rates of EoE in patients with IgE-FA previously described.<sup>1</sup> To our knowledge, this study is one of few efforts to formally screen for EoE symptoms in patients with IgE-FA. Although we focused on the presence of dysphagia, nearly all patients who met this end point also responded positively to at least 1 nondysphagia item, increasing clinical concern. In addition, more than half of the children reporting affirmatively to our supplemental question were also endorsing nondysphagia symptoms on the PEESS. Interestingly, positive responses to this question were lower in children with EoE, though we noted this subcohort to be small and that the symptoms may be influenced by factors such as current EoE treatment. Still, endorsement of dysphagia to any degree in children is notable, because this can be a late clinical manifestation of EoE and is often not present in pediatric patients. Moreover, the family history of EoE in 10% of the cohort was noteworthy, and may prove an important factor in screening. Finally, more than half of dysphagia cases were not simultaneously acknowledged by parents, suggesting that symptoms may be unrecognized and underreported both in the home and medical settings. Although a potential confounding factor, we did not find a large number of patients on oral immunotherapy with positive dysphagia responses (<2%).

Our findings are limited as a pilot study; we abbreviated the survey period to elicit initial baseline responses from our cohort as a foundation for future interventional studies. We did not include a

control group and did not pursue endoscopy to definitively diagnose EoE. Furthermore, we included an unvalidated supplemental question, although positive responses were associated with other positive items on the PEESS. In addition, we consider recent data suggesting that dysphagia scores on the PEESS may not differentiate EoE vs non-EoE groups<sup>10</sup>; however, this tool has been applicable historically and broadly in the research setting. Finally, we call attention to the possibility that esophageal eosinophilia may be asymptomatic and transient over time,<sup>5</sup> findings which must be fully considered alongside our data to limit the potential for overscreening, overdiagnosis, and unnecessary treatment.

In conclusion, children with IgE-FA and their parents report high rates of dysphagia concerning EoE. It is necessary to evaluate these patients histologically, but these findings may serve as the foundation for formal screening recommendations in the future. Clinicians should consider that EoE symptoms may go unnoticed by parents and physicians given the lack of formal screening.

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