ORIGINAL ARTICLE

The crucial role of allergists in the clinical management and treatment of eosinophilic esophagitis

Domenico Gargano[1], Laura Franceschini[2], Roberto Polillo[3], Carlo Maria Rossi[4,5], Donatella Bignardi[6], Danilo Villalta[7], Francesca Buzzulini[7], Gabriele Cortellini[8], Elena Pinter[9], Maria Beatrice Bilò[10,11], Alessandro Farsi[2]

[1]Allergy Unit, Azienda Ospedaliera S. Giuseppe Moscati, Avellino, Italy

[2]SOD Allergy and Clinical Immunology, Prato-Pistoia, Italy

[3]Allergologist, BIOS Spa, Rome, Italy

[4]Department of Internal Medicine and Medical Therapeutics, University of Pavia, Pavia, Italy

[5]First Department of Internal Medicine, Clinica Medica I, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy

[6]Allergology Unit, IRCCS San Martino Polyclinic Hospital, Genoa, Italy

[7]Immunology and Allergy Unit, S. Maria degli Angeli Hospital, Pordenone, Italy

[8]SSI Allergology Romagna Health Authority, Rimini Hospital, Rimini, Italy

[9]Clinic Immunology Unit, Policlinico Umberto I, Rome, Italy

[10]Allergy Unit, Department of Internal Medicine, University Hospital of Marche, Ancona, Italy

[11]Department of Clinical and Molecular Sciences, Marche Polytechnic University, Ancona, Italy

Summary

Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus affecting mainly young individuals with a high burden of comorbid atopic diseases and is associated with increased morbidity. Proton pump inhibitors (PPIs) is often the first line of treatment by inducing clinical remission in 30-50% of patients. Recently new drugs, such as budesonide orodispersible tablets and a monoclonal antibody targeting interleukin-4 and 13, have been found to be effective in clinical trials and approved to treat this condition.

A prompt diagnosis and correct management of these patients is of paramount importance to prevent fibrostenosis of the oesophagus and to improve the quality of life. The complex management of patients living with EoE requires the integrated cooperation of several specialists, including allergists, gastroenterologists, pathologists, dietitians, and psychologist.

Impact statement

The allergist plays a key role in coordinating the management of eosinophilic esophagitis, identifying individuals at risk to screening for related atopic comorbidities. The allergist is also primarily responsible for prescribing diet therapy in close collaboration with the dietitian. The purpose of this review is to clarify and highlight the importance of this role.

1. Introduction

Eosinophilic oesophagitis (EoE) is a chronic immune-mediated, allergen-driven disease of the oesophagus with a typical type-2 pattern of inflammation. Its epidemiology is rapidly increasing in the last decades, currently estimated to affect 1 in 1000-2000 individuals (1). EoE affects especially males patients, it has bimodal peak with most cases in either pediatric age group or the third-fourth decade of life. EoE, if unrecognized or improperly treated can lead to organ damage such as progression to fibrosis and harmful esophageal stenosis (2). Moreover, it is closely associated with other type 2 inflammatory disorders, including atopic dermatitis [AD], allergic rhinitis [AR], asthma, chronic rhinosinusitis with nasal polyps (CRSwNP) and food allergy [FA]. Therefore, managing patients with EoE and coexisting atopic diseases can be complex and requests a multidisciplinary approach (3).

The pathogenesis of EoE is multifactorial and results from the complex, still mostly undefined, interaction between genetics and intrinsic factors, environment, and antigenic stimuli. Epithelial barrier defects have long been recognized as a key factor in the development of EoE and other type-2 mediated diseases. A reduced expression of tight junction proteins and desmoglein-1, resulting in a loss of epithelial integrity, has been reported also for active EoE (4). Histological characteristics include dilated interepithelial spaces, basal cell hyperplasia, decreased desmosomes and a profound loss of esophageal tissue differentiation. The principal factors involved in these alterations are filagrin, calpain and epidermal differentiation complex. Subsequent to impaired barrier function, environmental factors, including microbes and their products (pathogen associated molecular patterns-PAMPs), allergens, or irritants, can induce immune responses by directly activating epithelial cells. Epithelial cytokines, such as TSLP, IL-25, and IL-33, can activate Innate Lymphoid Cells type 2 (ILC2) and promote T-helper Type 2 (Th2) cell differentiation. Th2 cells and ILC2 produce type 2 cytokines, including IL-4, IL-5, and IL-13, and promote the presence of other inflammatory mediators, orchestrating and

amplifying the inflammatory response by recruiting effector cells (eosinophils, basophils, and mast cells) and inducing the production of IgE. It has been also demonstrated that Th2 cytokines further damage the epithelial barrier favoring the worsening of its integrity (5). Several authors have noted elevated levels of IgG4 in EoE esophageal tissues (6; 7; 8). However, there are conflicting data on the role of IgG4 in EoE (6; 9; 10; 11). The diagnosis of EoE rests upon clinical symptoms (the most distinctive one being solid dysphagia with bolus impaction), together with the histopathologic finding of more than 15 eosinophils per high power field (HPF), in at least two different portions of the oesophagus and in the absence of secondary causes (12-14). In rare instances, such as with EoE-like diseases and EoE variants, eosinophils may be absent, while mast cells or lymphocytes could potentially play a pathogenetic role (15).

According to current guidelines,(16) the treatment of EoE is based upon first-line pharmacologic or dietary therapies, including proton pump inhibitors (PPI), food elimination diets and swallowed topical steroids. Dupilumab, a monoclonal antibody anti-IL4 e IL-13, is currently the only approved biologic for this condition in adults and adolescents older than 12 years weighing at least 40 kilograms, after attaining the coprimary endpoint of clinical and histological response in a phase 3 randomized clinical trial (18; 19). Recently, the Food and Drug Administration (FDA) approved dupilumab also for the treatment of EoE in children over the age of 1 year and weighing at least 15 kg.

Additional biologics that have been used to treat eosinophilic asthma and other type 2 conditions have also been tested for the treatment of EoE including monoclonal antibodies that target eosinophils by inhibiting IL-5 and IL-5 receptor. However, despite showing significant effects on eosinophil infiltration, these treatments did not result in a clinical response (20). Finally, elemental diets and oesophageal dilations are considered as rescue therapies.

However, despite numerous advancements in therapy, there are still significant unanswered questions regarding the management of EoE. This includes determining the optimal first-line therapy among various available options, the role of dupilumab in the treatment plan, and the proper timing for endoscopic and clinical monitoring of patients (21). According to FDA, dupilumab is recommended as a primary treatment option for EoE, without the need for trying other medications first, while according to a panel of Italian experts, dupilumab should be considered especially in patients inadequately controlled by first-line therapy, in patients with type 2 comorbidities, and in adolescents at risk of the use of swallowed corticosteroids. (22)

Prevalence of atopic disorders in patients with EoE

According to several lines of evidence, there is a strong association between EoE and atopic disorders. In a US-based retrospective administrative data study, the prevalence of asthma, AR, AD, and FA in the year following the diagnosis of EoE was estimated to be 44.7%, 27.1%, 25.2%, and 16.9, respectively (2). It is noteworthy that 63% of patients with EoE exhibited at least one of these allergic comorbidities, and 3% had all of them (23). A systematic review with meta-analysis revealed a significant correlation between EoE and allergic comorbidities, specifically allergic rhinitis and asthma (24).

In a more recent study using a retrospective registry in the US, focused on pediatric patients, it was discovered that the diagnosis of EoE often occurs after the diagnosis of other allergic conditions. This suggests that EoE may be considered a later stage in the progression of atopic diseases (25).

Remarkably, the presence of atopic comorbidities in EoE is so significant that it has been included in a predictive model for diagnosing EoE along with other demographic and clinical factors, such as young age, male gender, and pre-endoscopy dysphagia. This model has shown a sensitivity of 0.83 for predicting EoE. (26)

The role of yhe allergist in the diagnosis of T2-driven diseases

Diagnosing EoE in young male patients who experience bolus impaction is typically straightforward, however other symptoms of the disease can be more subtle and complex. These may include vomiting and abdominal pain in children, isolated reflux symptoms or mild difficulty swallowing due to behavioral adjustments such as altering food texture, consuming more fluids, and eating at a slower rate.

However, due to the significant link between type 2 inflammation disorders, allergists should be knowledgeable about the diagnosis of EoE in their daily clinical practice. They should actively screen for it using a case-finding approach in patients with atopic comorbidities who present with dysphagia, even if it is mild. If EoE is suspected, the patient should be referred to a gastroenterologist for further evaluation through endoscopy (Table 1). According to guidelines, it is recommended to discontinue PPI treatment 2 weeks before the exam in order to improve the detection of eosinophils in biopsy specimens of the esophagus (14).

The recent Italian consensus on EoE diagnosis underlined that in case of clinical suspicion of EoE, PPI should be withdrawn at least 3-4 weeks prior to endoscopy and biopsy collection to achieve an accurate diagnosis, although more data regarding the optimal timing of PPI withdrawal is needed (15)

One particular group of patients who are at risk for EoE are those who may be undergoing sublingual immunotherapy (SLIT) for respiratory allergies in both children and adults and those undergoing oral immunotherapy (OIT) for food allergies in pediatric settings. The incidence of EoE linked to allergen immunotherapy (AIT), meaning cases that develop after starting immunotherapy, is estimated to be around 2.7 - 3% (27). Currently, an ongoing European Academy of Allergy and Clinical Immunology Task Force is evaluating the true prevalence of this specific subtype of EoE and how best to manage it (28). In the majority of cases, remission of EoE is achieved by discontinuing AIT, while in other instances, pharmacological treatment with either PPI or swallowed topical steroids is initiated (46).

On the other hand, after diagnosing EoE, it is crucial to assess all patients for AR, asthma, AD, FA, and CRSwNP, if not previously done. This will help in selecting a treatment plan that can effectively address all areas of type 2 inflammation, such as with the use of dupilumab. For this reason patients initially evaluated by a gastroenterologist for dysphagia, should then undergo an allergy evaluation.

The allergy screening should include both in vivo and in vitro tests such as skin prick tests with inhalant and food allergens (if indicate prick by prick with fresh foods) and specific IgE determination, with extracts and molecular components. A future field of research currently open, may be the evaluation of the significance of Lipid Transfer Protein sensitisation in patients with eosinophilic oesophagitis.

Pulmonary function tests, nasal examination, and other evaluations to be performed in patients with EoE are outlined in Table 2.

Patients with EoE often show sensitization to multiple classes of respiratory and food allergens. The clinical manifestations can vary in severity, and symptoms can range from oral allergic syndrome to anaphylaxis when sensitization to food allergens is present. The co-occurrence of EoE and food allergy may have important implications on the management of the patient. Furthermore, patients who developed symptoms of EoE at a young age and those with allergic comorbidity are more likely to experience “food-induced immediate response of the esophagus (FIRE)”. This ischaracterized by a rapid and consistent occurrence of intense pain described as "burning, choking, or pressure" after consuming foods such as fruits and wine (29). The

underlying causes of the FIRE syndrome are currently not well understood, but it is unlikely to be related to an IgE-mediated mechanism. More broadly, based on current understanding, it appears that IgE-mediated reactions do not contribute to the pathogenesis of EoE. In this contest, it is notable that the prick test for food allergens or the determination of food-specific IgE have limited predictive ability in identifying the specific foods that trigger or exacerbate EoE. Additionally, the use of the anti-IgE monoclonal antibody omalizumab in treating patients with EoE did not lead to successful clinical outcomes (30).

The role of the allergist in the multidisciplinary management of EoE

Because EoE is a complex condition, it is necessary to have a specialized team of healthcare providers to properly care for patients. This team often consists of gastroenterologists, allergists, pulmonologists, otorhinolaryngologists, pathologists, dietitians, and psychologists. During the transitional period, it is important the involvements the pediatricians. (Figure 1). (31-33 -)

Effective communication and collaboration between the patient and the physician are crucial in the management of EoE, as the long-term treatments for chronic conditions necessitate a significant level of dedication and compliance. Indeed, poor adherence rates reach 41.8% according to a US study, already in the first year of therapy (34). Patient involvement in the management plan may define strategies that better suit the patient's need and improve adherence to therapy.

After an EoE diagnosis, allergists help determine an initial treatment plan, which may include dietary management, proton pump inhibitors (PPIs), swallowed corticosteroids, or biologics. Follow-up is typically scheduled within 6 to 12 weeks after starting treatment to assess early response and adjust therapy if needed.

Patients may choose to avoid medications and to prefer allergen-free diets, which are also known as food elimination diets. Recent expert opinions recommend starting with a limited elimination of specific food categories, such as wheat and animal milk and dairy, also known as the two-food elimination diet (2-FED). If clinical and pathological response is not achieved, one option is to take a step-up approach by progressively increasing the number of eliminated food categories. For example, starting with egg and soy in a four-food diet (4-FED), and finally eliminating nuts and fish/shellfish in the six-food elimination diet (6-FED) as well (35).

On the contrary, a 6-FED approach should not be instituted upfront, due to the high commitment required and the risk of inducing macro- and micronutrient deficiencies (36-39) (Table 1).

If anti-inflammatory pharmacological treatment is selected, PPIs are the preferred first-line treatment. If PPIs are not effective, the next treatment option is to use swallowed topical steroids. When using this second option, it is recommended to maintain a low dosage over a prolonged period, possibly indefinitely, due to the chronic nature of the disease (36).

The allergist should be mindful that when recommending PPI therapy sensitization profile of the patients should be to thoroughly evaluated. In fact, with the reduction of stomach acid production, allergens normally destroyed by gastric juices (e.g. PR-10 and profilins) may maintain their allergenicity and cause systemic reactions. (40).

In case of co-existing severe/difficult to control atopic dermatitis, asthma, CRwNP, according to expert opinions, an upfront treatment with dupilumab with the weekly schedule of 300 mg subcutaneously approved for EoE, is suggested, since it can target the whole spectrum of type 2-mediated inflammation (21- 41). Of note, according to a recent work, the regimen of 300 mg every other week, usually adopted to treat the aforementioned conditions, is not effective in EoE (18). In the absence of severe/difficult to control other comorbidities, biological therapy with dupilumab should be considered when the disease is refractory or when patients develop adverse effects to the other first-line treatments (22).

The multidisciplinary team should recommend actively monitor patients with EoE in order to optimize therapy, address potential side effects, and potentially enhance treatment adherence. Monitoring activity relies on a thorough assessment that includes clinical, endoscopic, and histological evaluations. It is important to mention that an upper gastrointestinal endoscopy should be conducted 8 to 12 weeks following the initiation of induction treatment, as well as after any significant modification in treatment. Subsequent follow-up endoscopies should then be scheduled every 12 to 24 months. However, some flexibility in the timing of these procedures is permitted (42). For instance, if symptoms persist or worsen in patients undergoing dietary elimination or pharmacologic treatment a repeat endoscopy with biopsy might be moved up to confirm histologic response. In this situation allergists may help to recommend further dietary adjustments, alternative medications, or biologic therapy.

In cases of recurrent symptoms, follow-up visits are scheduled more frequently (every 3 to 6 months) to guide modifications. Emerging therapies, such as biologics targeting eosinophilic inflammation (e.g., dupilumab), require close monitoring for efficacy and adverse effects.

The allergist should also be directly involved in monitoring the disease and checking for possible treatment-related side effects in particular the dupilumab-related eosinophila (43) This adverse event seems to be more prevalent in patients with severe asthma and/or CRSwNP, although it is mostly not linked to clinical symptoms or consequences and does not have any noticeable impact on treatment effectiveness (44). However, it is important to remark that no cases were reported in the studies that resulted in the approval of dupilumab for EoE. (18-19 ,). Large-scale population-based studies are required to confirm the safety of blocking IL4/IL13 in individuals with EoE. This is particularly important due to the more frequent dosing regimen of the drug in comparison to other type-2 pathologies.

Finally, for patients achieving disease remission, follow-up intervals may be extended to every 6 to 12 months, depending on symptom stability and adherence to treatment.

If patients remain asymptomatic with stable histologic findings, longer follow-up intervals (e.g., annually) may be considered.

CONCLUSION

The comprehensive care of patients with EoE necessitates the collaboration of multiple specialists and the implementation of a treatment plan. The allergist, with his expertise in managing type 2 inflammation across various systems, is well-equipped to lead this effort. He takes a systemic approach by recognizing the natural progression of the patient's condition known as the allergic march. This involves the gradual involvement of various organs starting from the skin then progressing to respiratory tract, and eventually affecting the digestive system.

The management strategy should be customized according to the individual patient's characteristics and evolving needs over the course of the disease. This personalized approach aims to accurately identify the most suitable therapy for each patient in a precision medicine framework, ultimately boosting treatment adherence and enhancing long-term clinical outcomes and quality of life for those affected by the disorder.

Declarations

Ethics approval and consent to participate. Not relevant.

Consent for publication. Not relevant.

Availability of data and materials. Not relevant.

Competing interests. The authors declare no conflict of interest.

Funding. None.

Contributions

Domenico Gargano, Laura Franceschini, Alessandro Farsi, Carlo Maria Rossi, Roberto Polillo contributed equally to the drafting of the manuscript, Donatella Bignardi, Danilo Villalta, Francesca Buzzulini, Gabriele Cortellini, Elena Pinter and Maria Beatrice Bilò contributed equally to the bibliography and in the revision of the manuscript.

References

1) Gratacós Gómez AR, Ortega SF, Cañas AP, Brito FF, Muñoz Rodriguez JR, Torrijos EG. Impact of environmental factors on the epidemiology of eosinophilic esophagitis in southwestern Europe (2007-2020). J Allergy Clin Immunol Glob. 2023 24;2(2):100088.
2) Dellon ES, Hirano I. Epidemiology and Natural History of Eosinophilic Esophagitis.Gastroenterology.2018;154(2):319-332.e3.
3) Capucilli P, Hill DA. Allergic Comorbidity in Eosinophilic Esophagitis: Mechanistic Relevance and Clinical Implications. Clin Rev Allergy Immunol. 2019;57(1):111-27.
4) Sherrill JD, Kc K, Wu D, Djukic Z, Caldwell JM, Stucke EM et al. Desmoglein-1 regulates esophageal epithelial barrier function and immune responses in eosinophilic esophagitis.Mucosal Immunol 2014;7:718–729.
5) Akdis, C.A. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions?. Nat Rev Immunol 21, 739–751 (2021).
6) Inage E., Furuta G.T., Menard-Katcher C., Masterson J.C. Eosinophilic esophagitis: Pathophysiology and its clinical implications. Am. J. Physiol. Gastrointest.LiverPhysiol. 2018;315:G879–G886.

7) Clayton F., Fang J.C., Gleich G.J., Lucendo A.J., Olalla J.M., Vinson L.A., Lowichik A., Chen X., Emerson L., Cox K., et al. Eosinophilic esophagitis in adults is associated with IgG4 and not mediated by IgE. *Gastroenterology.* 2014;147:602–609.

8) Schuyler A.J., Wilson J.M., Tripathi A., Commins S.P., Ogbogu P.U., Kruzsewski P.G., Barnes B.H., McGowan E.C., Workman L.J., Lidholm J., et al. Specific IgG4 antibodies to cow's milk proteins in pediatric patients with eosinophilic esophagitis. J Allergy Clin Immunol. 2018;142:139–148.

9) Franceschini L, Biviano I, Malaspina L, Macchiarelli R, Farsi A. Eosinophilic esophagitis despite isolated IgG4 deficiency: The still unsolved conundrum of pathogenesis. Ann Allergy Asthma Immunol. 2023 Oct;131(4):525-526.

10) Franceschini L., Farsi A. IgG4 and eosinophilic esophagitis: Bridging the knowledge gap. J Allergy Clin Immunol. Volume 155, Issue 1p239-240 January 2025.

11) Appanna R, Gargano D, Caputo A, De Bartolomeis F, Ricciardi L, Santonicola A, Stefanelli B, Caiazza L, Guarciariello M, D'Antonio A, D'Auria R, Conti V, Casolaro V, Iovino P. Changes in mucosal IgG4+- and IL-10+-cell frequencies in adults with eosinophilic esophagitis on a two-food elimination diet. Clin Immunol. 2023 Dec;257:109853.

12) Dhar A, Haboubi HN, Attwood SE, Auth MKH, Dunn JM, Sweis R, et al. British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. Gut. 2022;71(8):1459-87.

13) Lucendo AJ, Molina-Infante J, Arias Á, von Arnim U, Bredenoord AJ, Bussmann C, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. United European Gastroenterol J. 2017;5(3):335-58.

14) Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit Net al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. Gastroenterology. 2018;155 (4):1022-33.e10.

15) Greuter T, Straumann A, Fernandez-Marrero Y, et. al. Characterization of eosinophilic esophagitis variants by clinical, histological, and molecular analyses: A cross-sectional multi-center study. Allergy. 2022 Aug;77(8):2520-2533. doi: 10.1111/all.15233. Epub 2022 Feb 17.

16) Dellon, Evan S., Muir, Amanda B., Katzka, David A., Shah, Shailja C. et.al ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. The American Journal of Gastroenterology 120(1):p 31-59, January 2025.

17) De Bortoli N, Visaggi P, Penagini R, et al. The 1st EoETALY Consensus on the Diagnosis and Management of Eosinophilic Esophagitis - Definition, Clinical Presentation and Diagnosis. Dig Liver Dis. 2024;56(6):951-963.

18) Dellon ES, Rothenberg ME, Collins MH, Hirano I, Chehade M, Bredenoord AJ,. Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis. N Engl J Med. 2022;387(25):2317-30.

19) Rothenberg ME, Dellon ES, Collins MH, Hirano I, Chehade M, Bredenoord AJ, et al. Efficacy and safety of dupilumab up to 52 weeks in adults and adolescents with eosinophilic oesophagitis (LIBERTY EoE TREET study): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Gastroenterol Hepatol. 2023;8(11):990-1004.

20) Rossi CM, Lenti MV, Di Sabatino A. Toning down the role of eosinophils in eosinophilic oesophagitis. Gut. 2023:gutjnl-2023-329864.

21) Aceves SS, Dellon ES, Greenhawt M, Hirano I, Liacouras CA, Spergel JM. Clinical guidance for the use of dupilumab in eosinophilic esophagitis: A yardstick. Ann Allergy Asthma Immunol. 2023 Mar;130(3):371-8.

22) Savarino EV, Barbara G, Bilò MB, De Bortoli N, Di Sabatino A, Oliva S, et al. Eosinophilic esophagitis in adults and adolescents: epidemiology, diagnostic challenges, and management strategies for a type 2 inflammatory disease. Therap Adv Gastroenterol. 2024 May 27;17:17562848241249570

23) Benninger MS, Strohl M, Holy CE, Hanick AL, Bryson PC. Prevalence of atopic disease in patients with eosinophilic esophagitis. Int Forum Allergy Rhinol. 2017;7(8):757-62.

24) González-Cervera J, Arias Á, Redondo-González O, Cano-Mollinedo MM, Terreehorst I, Lucendo AJ. Association between atopic manifestations and eosinophilic esophagitis: A systematic review and meta-analysis. Ann Allergy Asthma Immunol. 2017;118(5):582-590.e2.

25) Hill DA, Grundmeier RW, Ramos M, Spergel JM. Eosinophilic Esophagitis Is a Late Manifestation of the Allergic March. J Allergy Clin Immunol Pract. 2018;6(5):1528-33.

26) Cotton CC, Betancourt R, Randall C, Perjar I, Bookhout C, Woosley JT, et al. A Model Using Clinical and Endoscopic Characteristics Identifies Patients at Risk for Eosinophilic Esophagitis According to Updated Diagnostic Guidelines. Clin Gastroenterol Hepatol. 2021;19(9):1824-1834.e2.

27) Cafone J, Capucilli P, Hill DA, Spergel JM. Eosinophilic esophagitis during sublingual and oral allergen immunotherapy. Curr Opin Allergy Clin Immunol. 2019 Aug;19(4):350-357.

28) Pitsios C, Rossi CM, Terreehorst I, Heffler E, Votto M, Konstantinou GN, et al Eosinophilic esophagitis as a side-effect of allergen immunotherapy: protocol for a systematic review and meta-analysis.Eur Ann Allergy Clin Immunol. 2024 Jan;56(1):4-8.

29) Biedermann L, Holbreich M, Atkins D, Chehade M, Dellon ES, Furuta GT, et. al. Food-induced immediate response of the esophagus-A newly identified syndrome in patients with eosinophilic esophagitis. Allergy. 2021 Jan;76(1):339-347..

30) Franceschini L, Macchiarelli R, Biviano I, Farsi A. Eosinophilic Esophagitis Onset Despite Six Years' Treatment With Omalizumab in an Asthmatic Patient: No Protective Effect for Anti-IgE Therapy?. The American Journal of Gastroenterology 116(7):p 1560, July 1, 2021.

31) Robinson J, Furuta GT, Hadker N, Kolev I, Williams J, Juethner S, et.al Transition of Care from Pediatric to Adult Care in Eosinophilic Esophagitis: Insights From a Patient Perspective Survey. J Pediatr Gastroenterol Nutr. 2021 Dec 1;73(6):722-726.

32) Eluri S, Book WM, Kodroff E, Strobel MJ, Gebhart JH, Jones PD, et. Al Lack of Knowledge and Low Readiness for Health Care Transition in Eosinophilic Esophagitis and Eosinophilic Gastroenteritis. J Pediatr Gastroenterol Nutr. 2017 Jul;65(1):53-57.

33) Hiremath G, Chapa-Rodriguez A, Katzka DA, Spergel JM, Gold B, Bredenoord AJ, et al. Transition of care of patients with eosinophilic gastrointestinal diseases: Challenges and opportunities. Transl Sci Rare Dis. 2022;6(1-2):13-23.

34) Haasnoot ML, Safi S, Bredenoord AJ. Poor Adherence to Medical and Dietary Treatments in Adult Patients With Eosinophilic Esophagitis. Am J Gastroenterol. 2022;117(9):1412-18.

35) Mayerhofer C, Kavallar AM, Aldrian D, Lindner AK, Müller T, Vogel GF. Efficacy of Elimination Diets in Eosinophilic Esophagitis: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2023 Aug;21(9):2197-2210.e3.

36) Feo-Ortega S, Lucendo AJ. Evidence-based treatments for eosinophilic esophagitis: insights for the clinician. Therap Adv Gastroenterol. 2022.

37) Votto M, De Filippo M, Lenti MV, Rossi CM, Di Sabatino A, Marseglia GL, et al Diet Therapy in Eosinophilic Esophagitis. Focus on a Personalized Approach. Front Pediatr. 2022;9:820192.

38) Rossi CM, Lenti MV, Merli S, Cena H, Di Sabatino A. Dietary Strategies in Adult Patients with Eosinophilic Esophagitis: A State-of-the-Art Review. Nutrients. 2023;15 (10):2409.

39) Gargano D, Appanna R, Santonicola A, De Bartolomeis F, Stellato C, Cianferoni A, et al. Food Allergy and Intolerance: A Narrative Review on Nutritional Concerns. Nutrients. 2021 May 13;13(5):1638.

40) Asero R, Ariano R, Aruanno A, Barzaghi C, Borrelli P, Busa M, et al. Systemic allergic reactions inuced by labile plant-food allergens: Seeking potenzial cofactors. A multicenter study. Allergy 2021; 76 (5): 1473-1479.

41) Franceschini L, Farsi A. Eosinophilic oesophagitis and type 2 inflammation multimorbidity: an opportunity for biologic treatment. Lancet Gastroenterol Hepatol. 2022;7(9):787-8.

42) Arnim UV, Biedermann L, Aceves SS, Bonis PA, Collins MH, Dellon ES, et al. Monitoring Patients With Eosinophilic Esophagitis in Routine Clinical Practice - International Expert Recommendations. Clin Gastroenterol Hepatol. 2023 ;21(10):2526-2533.

43) Olaguibel JM, Sastre J, Rodríguez JM, Del Pozo V. Eosinophilia Induced by Blocking the IL-4/IL-13 Pathway: Potential Mechanisms and Clinical Outcomes. J Investig Allergol Clin Immunol. 2022;32 (3):165-80.

44) Wechsler ME, Klion AD, Paggiaro P, Nair P, Staumont-Salle D, Radwan A, et. Al Effect of Dupilumab on Blood Eosinophil Counts in Patients With Asthma, Chronic Rhinosinusitis With Nasal Polyps, Atopic Dermatitis, or Eosinophilic Esophagitis. J Allergy Clin Immunol Pract. 2022 Oct;10(10):2695-2709.

45) Egan M, Atkins D. What Is the Relationship Between Eosinophilic Esophagitis (EoE) and Aeroallergens? Implications for Allergen Immunotherapy. Curr Allergy Asthma Rep. 2018;18(8):43.

46) Wilson BE, Sacta MA, Wright BL, Spergel J, Wolfset N. The Relationship Between Eosinophilic Esophagitis and Immunotherapy. Immunol Allergy Clin North Am. 2024 May;44(2):281-291.

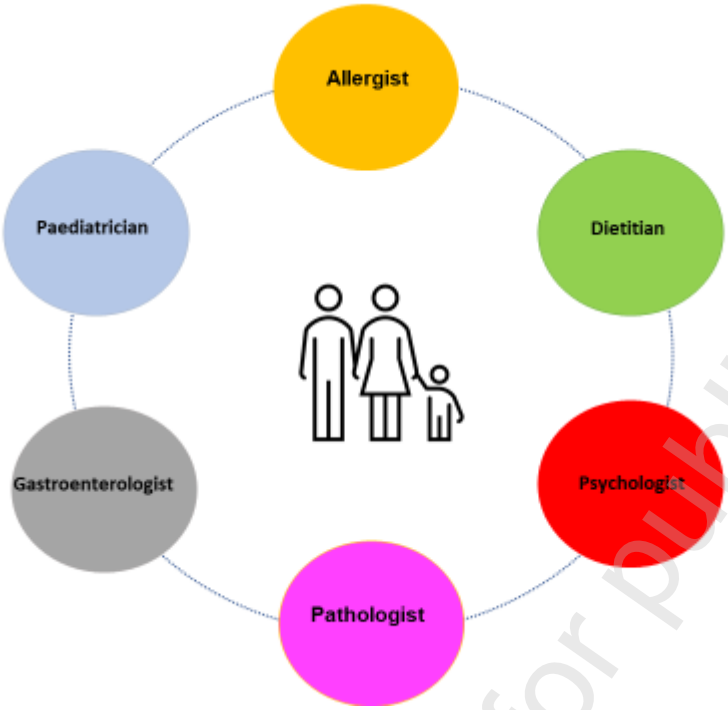

Figure 1
The complex care of patient with EoE requires the cooperation of several professional figures including the allergist, the gastroenterologist, the pathologist, the dietitian, the psychologist and often the paediatrician. The interaction between these professionals is suggested by the circle. The interaction between the allergist for adults and a paediatrician is especially important in the transition age.

Table I The role of the allergist in the diagnosis and management of EoE

Diagnosis
-Screening for EoE patients at risk for EoE (for example in young male patients with atopic comorbidities, presenting with dysphagia on in patients undergoing SLIT or OIT presenting with dysphagia or reflux symptoms)
-Screening of atopic co-morbidities in patients with established diagnosis of EoE
Management
-Consideration of IgE-mediated food allergies, before allergen-free diet prescription
-Consideration of FIRE syndrome in young atopic patients
-Attention when prescribing PPI, if sensitization to PR-10 or profilin is present
-Monitoring side effects of therapies (oesophageal candidosis, dupilumab-related eosinophilia, dupilumab-related ocular disease)
-Monitoring the occurrence of new onset food allergies in patients undergoing allergen-free diets
Oral or sublingual immunotherapy discontinuation, pharmacological treatment, change of administration route of AIT (from sublingual to subcutaneous) in cases of sublingual AIT-associated EoE