ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Clinical characterization and first-line treatment response in patients with eosinophilic esophagitis: experience from a Portuguese Immunoallergology department

Caracterização clínica e resposta ao tratamento de primeira linha em doentes com esofagite eosinofílica: experiência de um serviço português de imunoalergologia

Ana Graça Bernardino[1], Margarida Gomes[1], Célia Costa[1,2]

RESUMO

Introdução: A esofagite eosinofílica (EoE) é uma doença crônica imunoalérgica de patogênese ainda pouco compreendida. O tratamento visa controlar os sintomas e a inflamação, mas a resposta às terapêuticas de primeira linha permanece pouco esclarecida. Este estudo teve como objetivo caracterizar uma coorte de doentes com EoE, avaliar a eficácia das terapêuticas convencionais e determinar eventuais biomarcadores de resposta. **Métodos:** Estudo retrospetivo de doentes com EoE seguidos entre 2009 e 2023. **Resultados:** Foram incluídos 130 doentes com EoE, 79,2% do sexo masculino, com idade mediana (IQR) de 24 (18) anos. A idade mediana (IQR) do início dos sintomas foi de 13 (15) anos e do diagnóstico, de 17 (18,5) anos. O intervalo médio entre o início dos sintomas e o diagnóstico foi de 49 meses. O impacto alimentar e a disfagia foram os sintomas mais frequentes, em 72,3% e 66,2% dos doentes, respetivamente. Doença clínica grave foi observada em 51,5% e doença histológica grave em 42,3%. Comorbilidades atópicas estavam presentes em 84% dos doentes, sensibilização alimentar em 67% e sensibilização a aeroalérgenos em 80,8%. Relativamente à resposta terapêutica, 20,8% foram considerados respondedores completos (G1), 9,2% não respondedores (G2), 64,6% respondedores parciais(G3) e 5,4% aguardavam avaliação endoscópica e/ou histológica. No grupo G3, 65,5% mantinham sintomas; 94% apresentavam alterações endoscópicas e 88,4% apresentavam alterações histológicas. As opções terapêuticas entre G1 vs G2, G1 vs G3 ou G1 vs G2 + G3 não apresentaram diferenças estatisticamente significativas. Na comparação G1*vs*G2+G3, observaram-se diferenças significativas nos eosinófilos periféricos (360 vs 530/μL, p=0,047) e na presença de doença histológica grave (18,5% vs 51%, p=0,003). **Conclusões:** A maioria dos doentes era do sexo masculino, com um atraso médio de quatro anos desde o início dos sintomas. Apenas 21% alcançaram remissão completa com terapêuticas de primeira linha. Níveis basais elevados de eosinófilos periféricos e doença histológica grave associaram-se a

ABSTRACT

Background: Eosinophilic Esophagitis (EoE) is a chronic immune- and allergen-mediated disease with incompletely understood pathogenesis. Treatment aims to relieve symptoms, control inflammation, prevent complications, and improve the quality of life. Despite first-line therapies, the treatment response remains poorly understood. This study aimed to characterize an EoE cohort, evaluate the effectiveness of conventional treatments, and determine possible biomarkers of response. **Methods:** We conducted a retrospective study of patients with EoE who were followed up from 2009 to 2023. **Results:** A total of 130 patients with EoE were included: 79.2% were male, and the median (IQR) age was 24 (18) years. The median (IQR) age at symptom onset was 13 (15) years and at diagnosis was 17 (18.5) years. The mean time gap between symptom onset and diagnosis was 49 months. Food impaction and dysphagia were the most frequent symptoms, 72.3% and 66.2%. Of these, 51.5% had severe clinical disease, and 42.3% had histologically severe disease. Of the patients, 84% had atopic comorbidities, 67% had food sensitization, and 80.8% had aeroallergen sensitization. Regarding therapeutic response, 20.8% were complete responder (G1), 9.2% non-responder (G2), 64.6% partial responders(G3), and 5.4% were awaiting evaluation. In G3,65.5% maintained symptoms, 94% endoscopic, and 88.4% histological abnormalities. Therapeutic G1*vs*G2, G1*vs*G3 or G1*vs*G2+G3 did not show significant differences. In G1*vs*G2+G3, significant differences were observed in peripheral eosinophils (360vs530/ul, p=0.047) and histologically severe disease (18.5vs51%, p=0.003). **Conclusions:** Most patients were male, with a mean delay of 4 years from the symptom onset. Only 21% of patients achieved complete remission with first-line therapy. High baseline peripheral eosinophil levels and severe histological disease were associated with partial/no response to first-line treatments,

[1]Hospital de Santa Maria, Unidade Local de Saúde de Santa Maria, Serviço de Imunoalergologia - Lisboa, Portugal.
[2]Universidade de Lisboa, Faculdade de Medicina, Clínica Universitária de Imunoalergologia - Lisboa, Portugal.

resposta parcial ou ausente às terapêuticas de primeira linha, sendo necessários mais estudos para esclarecer a imunopatogênese da EoE e identificar biomarcadores preditivos.

Descritores: Esofagite eosinofílica; eosinófilos; terapêutica; resultado do tratamento; biomarcadores.

suggesting distinct pathophysiological mechanisms. Further studies are needed to clarify the immunopathogenesis of EoE and to identify predictive biomarkers.

Keywords: Eosinophilic esophagitis; eosinophils; therapeutics; treatment outcome; biomarkers.

Introduction

EoE is a complex, heterogeneous, and chronic immune-mediated inflammatory disorder that is often progressive[1-3]. It was first described in 1978 and later defined by Attwood et al.[2] in 1993 and Straumann et al.[4] in 1994. The pathophysiological mechanism is still not fully understood and is likely multifactorial, involving an abnormal esophageal response to food and/or environmental allergens in genetically predisposed individuals, along with epithelial barrier alterations and possibly esophageal microbiota changes[3,5-7].

Foods such as milk, eggs, wheat, and soy trigger disproportionate immune responses, contributing to chronic esophageal inflammation[6-8].

Th2 interleukins (IL), particularly IL-4, IL-5, and IL-13, play a central role, increasing eotaxin 3, recruiting and activating eosinophils, basophils, and mast cells, and promoting chronic inflammation, tissue damage, fibrosis, and dysmotility with smooth muscle constriction[1,3,7,9] .

EoE is diagnosed based on mucosal eosinophilic infiltration of ≥15 eosinophils per high-power field (eos/hpf) in the esophagus, along with symptoms of esophageal dysfunction, after excluding other conditions with similar clinical, histologic, or endoscopic features[1,10-13].

Symptoms vary by age: in adults, dysphagia, gastroesophageal reflux, heartburn, and food impaction are most common, reflecting progression toward esophageal stenosis; in children, vomiting, regurgitation, heartburn, and abdominal pain are more frequent[7,13,14].

Treatment aims to control symptoms, restore quality of life and oral intake, and reduce inflammation to prevent irreversible changes. The choice of initial therapy involves considering the reported efficacy, patient preferences, disease severity, and resource availability.

Current guidelines from the American Gastroenterological Association (AGA) and the Joint Task Force on Allergy-Immunology Practice Parameters (JTF) recommend swallowed topical corticosteroids (STC) as the first-line therapy, with a strong recommendation supported by moderate-quality evidence[10,12]. High-dose proton pump inhibitors (PPI) can also be effective and safe, representing a viable initial option for many patients[10,12].

An elimination diet is another first-line option recommended, although it is considered a conditional recommendation due to low-quality evidence. Current strategies include elemental and empirical or target elimination diets. There may be challenges with long-term adherence to dietary elimination and a major limitation to the use these diets in treatment of EoE is the need for repeated endoscopic biopsy assessment during the food reintroduction process[10,12,16].

Recently, dupilumab, a humanized monoclonal antibody that blocks the IL-4 receptor alpha chain and modulates IL-4/IL-13 signaling, was approved for EoE in patients aged ≥12 years when conventional therapies fail[17,18].

Endoscopic dilation may be considered in severe stenotic cases to reduce the risk of food impaction; however, it does not improve histologic eosinophilia[10,12].

Whenever possible, management should involve a multidisciplinary team, including immunoallergologists, gastroenterologists, and nutritionists, to assess dietary feasibility and ensure nutritional follow-up[12,16].

In this context, we aimed to characterize a cohort of patients with EoE followed in the Immunoallergology department of a tertiary Portuguese hospital over a 13 years period, providing a detailed description of their clinical profile and assessing the effectiveness of conventional treatment approaches tailored to evolving guidelines and patient or family preferences.

Material and methods

This was a retrospective, observational, real-life study of patients with EoE followed up at a tertiary center from January 2009 to December 2023. Demographic and clinical data were obtained from the clinical records of all patients.

We analyzed demographic data, symptoms reported, and personal history of allergic diseases. A personal history of allergic diseases was defined as the presence of a previous physician-diagnosed allergic condition (asthma, allergic rhinitis, atopic dermatitis, or food allergy), supported by clinical history and confirmatory skin prick test.

Additionally, we considered serum total IgE and peripheral eosinophil values, sensitization to inhaled allergens (assessed through skin prick testing using a standard commercial panel adopted by our department), and food sensitization (determined by skin prick tests with both the standard commercial panel and additional allergens based on patient symptoms, as well as atopy patch testing with a fresh food panel used in our department). We also considered clinical disease severity, histological severity, and response to conventional treatment, which included PPI (up to 30 mg twice daily for lansoprazole and 40 mg twice daily for other PPIs in adults, and 1 mg/kg per dose twice daily in children), STC (fluticasone up to 1500 µg/day in adults and 1000 µg/day in children), and allergy-test-guided elimination diet. These interventions were implemented according to our department's treatment algorithm (Figure 1), which has been adapted over time to incorporate evolving guidelines and tailored to the preferences of the patient or their families.

Skin prick tests (SPT) were performed for common aeroallergens with commercial extracts (Bial-Aristegui®, Bilbao, Spain), namely house dust and storage mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Euroglyphus maynei*, *Lepidoglyphus destructor*, *Blomia tropicalis*, *Glycyphagus domesticus*, *Acarus siro*, *Tyrophagus putrescentiae*), dog and cat's fur, *Alternaria alternata*, *Aspergillus fumigatus*, mixtures of grasses, *Phleum pratense*, *platanus*, *Olea europaea*, *Parietaria judaica*, *Artemisia vulgaris* and *Plantago lanceolata*. Patients underwent SPT with selected foods according to their clinical history suggestive of IgE-mediated food allergy, in addition to a standard panel of milk and proteins (alfa-lactoalbumin, beta-lactoglobulin, casein), soy, egg (yolk, white, ovalbumin, ovomucoid), meats (beef, chicken, turkey, pork, and rabbit), fish (bream, hake, sea bass, sardine, horse mackerel, cod, tuna, and salmon), seafood (shrimp), cereals (rice, wheat, barley, corn, rye, and oat), fresh fruits (apple, pear, and peach), tree nuts (walnut, hazelnut, cashew, almond, chestnut, pistachio, and pinion), and peanuts. SPT was performed by an appropriately trained and experienced professional. The positive control was performed using histamine dihydrochloride (10 mg/ml), and the negative control was performed using an isotonic saline solution. The SPT results were read after 15 min by measuring the wheals (mm) using a graduated ruler. Papules with an average diameter measuring 3 mm larger than the negative control were considered positive[19].

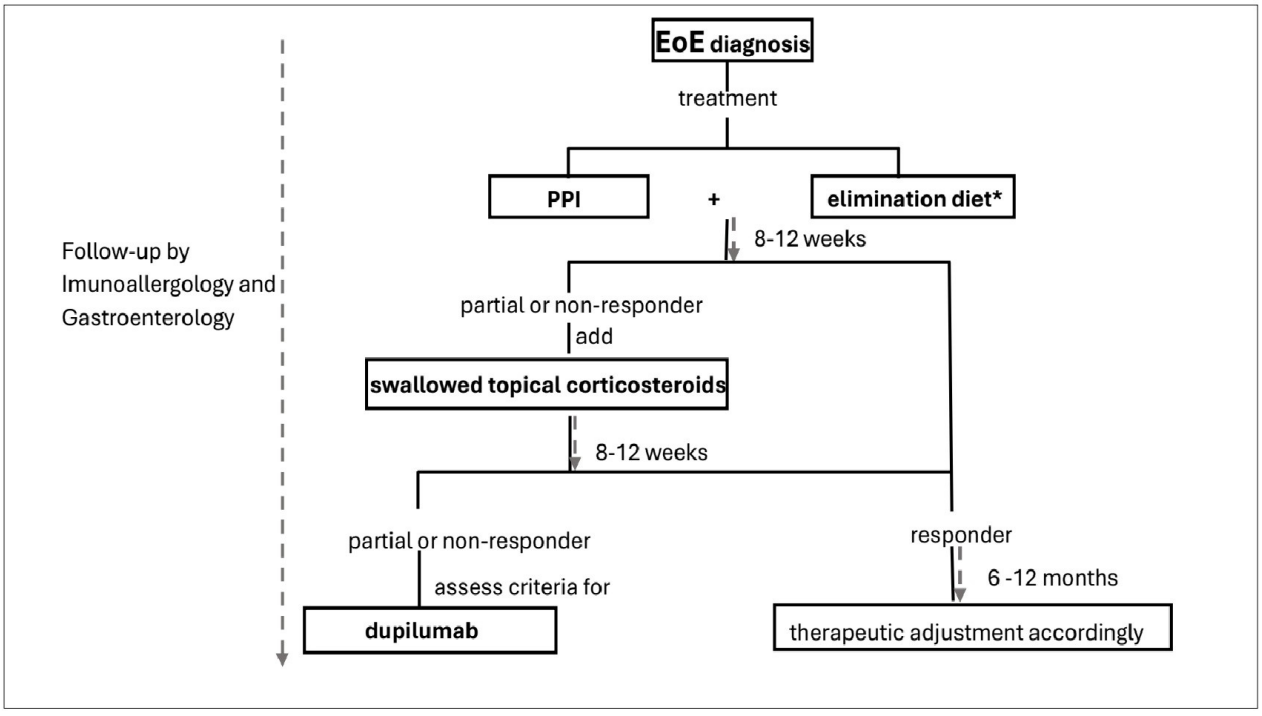

Figure 1
Therapeutic algorithm for patients with EoE adopted in the department. *allergy-test-based elimination diet; PPI - high dose of Proton Pump Inhibitor

Food atopy patch tests were performed using the following standard fresh foods: cow's milk, egg white (raw and cooked), egg yolk (raw and cooked), wheat flour, cornflour, walnut, hazelnut, cashew, almond, pistachio, pinion, beef, pork, chicken, turkey, shrimp (raw and cooked), hake, codfish, and soy. The foods were mixed with isotonic saline and placed in aluminum cups (8-mm Finn Chambers® in Scanpor tape; Smartpractice Europe GmBH, Germany) and adhered to the patient's back. The patches were removed at 48 h, and the results were read at 48 and 96 h. Reactions were classified as + for erythema and scattered papules, ++ for erythema and papules, and +++ for erythema and vesicles, according to standard patch testing protocols[20].

Severe clinical disease was characterized by at least one visit to the emergency department or hospital admission due to EoE complications (severe dysphagia, food impaction, or esophageal perforation). The criteria for defining EoE complications were adapted from Furuta and Katzka[21] and Gomez Torrijos et al.[22].

Histological severe disease was considered if it was observed equal to or greater than 55 eos/hpf and/or microabscesses in esophageal biopsies. These criteria were adapted from van Rhijn et al.[23].

When evaluating the patient's response to treatment, we categorized the patient into one of three groups based on the following criteria, adapted from Dellon and Gupta[24]: 1. Complete responder (G1): Patient-reported symptom resolution, as well as normalization of endoscopic and esophageal biopsies (<1eos/hpf). 2. Non-responders (G2): Persistence of symptoms, esophageal eosinophilia (>15eos/hpf), and endoscopic abnormalities. 3. Partial responder (G3): Persistence of symptoms and/or continued observation of endoscopic or histological abnormalities.

Following the classification of patients based on their response to treatment, we compared the frequency of patients exhibiting different treatment responses within the same therapeutic strategy (G1 vs. G2, G1 vs. G3, and G1 vs. G2+G3).

The analyzed variables, (gender, age at onset of symptoms, age at diagnosis, time gap between onset of symptoms and diagnosis, personal history of allergic diseases, serum total IgE and eosinophil values, food sensitization, clinical disease severity, histologically severe disease, and response to treatment within the same treatment approaches), between G1 and the combined group of G2 and G3.

Statistical analyses were performed using IBM SPSS software (version 21.0; IBM Corp.). Continuous variables are presented as means and standard deviations or medians and interquartile ranges for variables with skewed distributions, and categorical variables are presented as frequencies and percentages. Normal distribution was confirmed using the Shapiro-Wilk test or skewness and kurtosis. For bivariate analysis, the t-independent test or Mann-Whitney test was used to compare parametric and non-parametric variables, respectively. Categorical variables were compared using Fisher's exact test or Pearson's chi-square (χ^2) test, as appropriate. Statistical significance was set at $p < 0.05$.

This study was conducted in accordance with the ethical and legal principles and followed the recommendations of the Declaration of Helsinki of the World Medical Association. The anonymity of all participants in this study was guaranteed.

Results

A total of 130 patients with eosinophilic esophagitis were included, of whom 103 were male (79.2%), with a currently median(IQR) age of 24[18] years, being 19 patients (14.6%) under 18 years. As also observed in Table 1, the median (IQR) age at the onset of symptoms was 13[15] years and at diagnosis 17 (18.5) years.

The mean±SD time gap between the onset of symptoms and diagnosis was 49±65.7 months. For 73 patients (56.2%) diagnosis was established at a pediatric age and in 57 (43.8%) patients at adult age.

Most patients (83.8%; n=109) had atopic comorbidities: 79.2% had allergic rhinoconjunctivitis, 30.8% had IgE-mediated food allergy, 26.2% had asthma, and 11.7% had atopic dermatitis.

Food sensitization was observed in 66.9% (n=87) of the patients, with more relevance to tree nuts (n=26, 20%), cow's milk (n=22, 16.9%), wheat (n=20, 15.4%), and egg (n=19, 14.6%).

Skin prick tests with airborne allergens were positive in 105 (80.8%) patients, with greater relevance to house dust mites (n=92, 70.8%) and pollen (n=70, 53.8%).

According to Figure 2, the most frequent symptoms reported were food impaction (72.3%), followed by dysphagia (66.2%), retrosternal pain (40%), gastroesophageal reflux (25.4%), and vomiting (23.8%). At the time of diagnosis, both median blood serum eosinophil count and total IgE level were above the reference values, 476 cells/uL and 164 KU/L, respectively.

Table 1
Characterization of study population

Treatments	Total Patients n=130	Complete Responders (G1) n=27	Non Responders (G2) + Parcial Responders (G3) n=96	G1 *vs*(G2+G3) *p* value
Male, %	79.2	70.4	81.3	0.22#
Median age, Y(IQR)	24(18)	26(14)	24(20)	0.76*
Median age at onset of symptoms, Y(IQR)	13(15)	12(10)	14(15)	0.6*
Median age at diagnosis, Y(IQR)	17(18.5)	16(15)	17(20)	0.29*
Mean time gap between onset of symptoms and diagnosis, months±SD	49±65.7	45±82.3	50.9±60.6	0.5**
Personal history of allergic diseases, %	83.8	85.2	83.3	0.63#
Median blood serum eosinophils, cells/uL(IQR)	476(350)	360(338)	530(360)	**0.047***
Median serum total IgE, KU/L (IQR)	164(651)	180(514.6)	145(516,5)	0.89*
Food sensitization, %	66.9	70.4	64.6	0.8#
Severe clinical disease, %	51.5	44.4	56.3	0.3#
Histologic severe disease, %	42.3	18.5	51	**0.003#**

***Mann Whitney statistic test. **T-test statistic test. #Chi-square statistic test.**

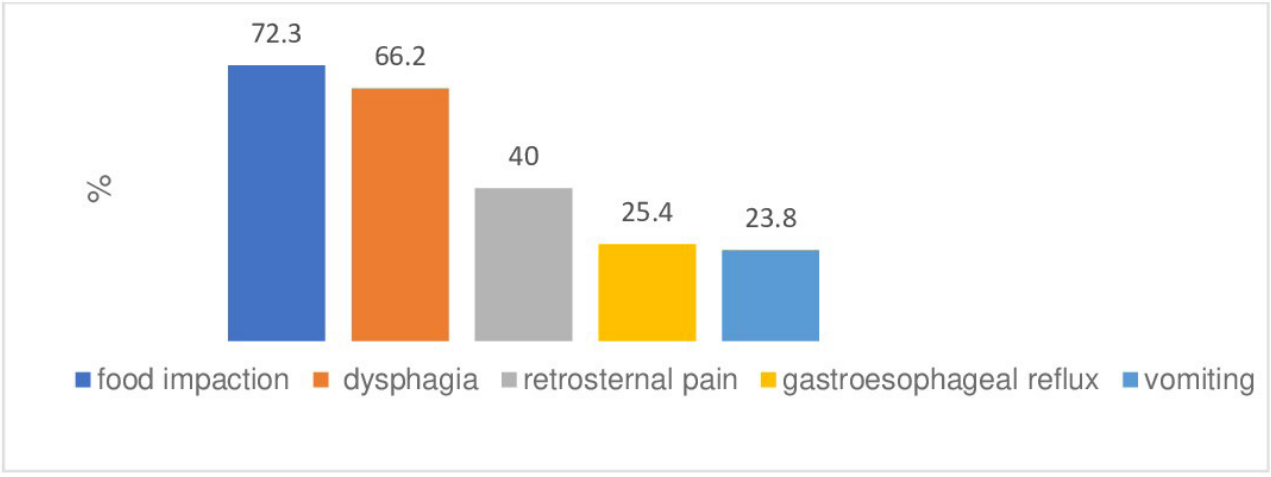

Figure 2
Eosinophilic esophagitis symptoms at diagnosis

At the time of EoE diagnosis, 51.5% (n=67) had severe clinical disease and 42.3% (n=55) had severe histological disease.

Globally, most patients (64.6%) were partial responders (G3), of whom 65.5% maintained symptoms and 93.9% and 88.4% had endoscopic and histologic abnormalities, respectively. Nevertheless, 20.8% of the patients achieved a complete response (G1), 9.2% maintained non-response, and the remaining 5.4% had not yet undergone endoscopic and/or histological evaluation (Figure 3).

According to the treatment algorithm used in our department, the following distribution of patients was observed (also detailed in Table 2): 79.2% received optimized therapy with swallowed fluticasone combined with PPI, either with (55.2%) or without (24%) an eviction diet; 14.4% were treated exclusively with PPI, of whom 5.6% also followed an eviction diet; and 6.4% were on therapeutic regimens without PPI, which was not initially considered in the algorithm, with half of these patients (3.2%) also on an eviction diet.

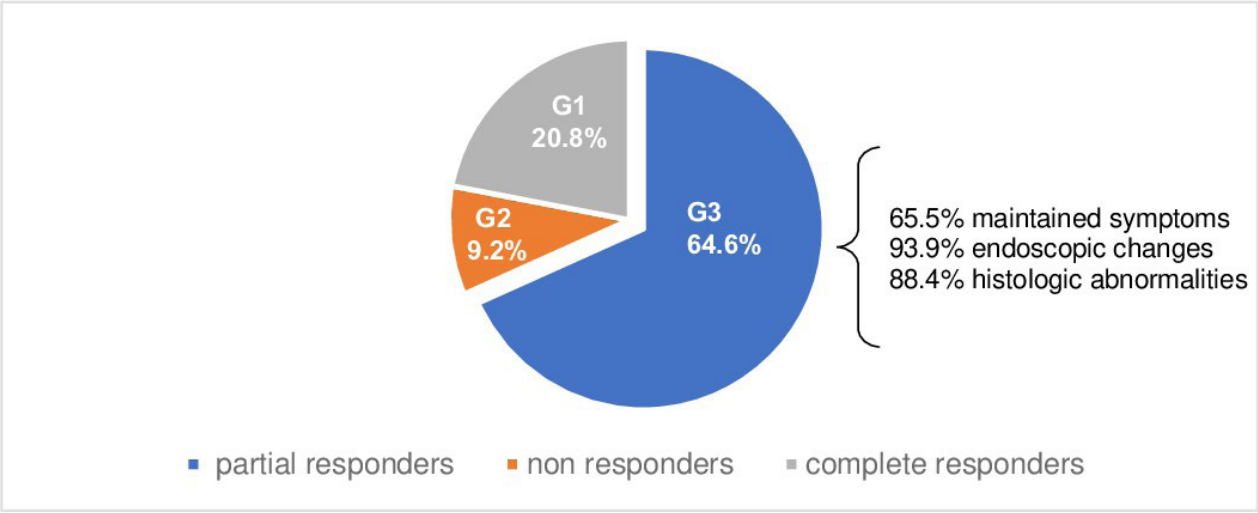

Figure 3
Classification of treatment response

Table 2
Treatments approaches in patients with eosinophilic esophagitis and comparation between groups

Treatment	Total Patients (%)	Complete Responders (G1) (%)	Non Responders (G2), (%)	Parcial Responders (G3), (%)	G1 *vs* G2, $p^{\#}$	G1 *vs* G3, $p^{\#}$	G1 *vs* (G2+G3), $p^{\#}$
SF + PPI + ED	55.2	59.3	54.5	53.6	0.79	0.66	0.66
SF+PPI	24	14.8	45.5	25	0.1	0.42	0.21
PPI+ED	5.6	7.4	0	4.8	-	0.63	0.61
SF+ED	3.2	3.7	0	3.6	-	0,97	0.88
Isolated PPI	8.8	7.4	0	10.6	-	0.61	0.74
Isolated SF	3.2	7.4	0	2.4	-	0.25	0.21

ED - Elimination Diet; PPI- high dose of Proton Pump Inhibitor; SF - Swallowed Fluticasone. #Chi-square statistic test.

These therapeutic options reflect patient or family preferences and adjustments made in response to disease remission during prior evaluations.

The response to the established therapeutic regimens can be found in Table 2, where no statistical differences were observed in the frequency of patients between G1 *vs* G2, G1 *vs* G3, or G1 *vs* G2+G3 within the same therapeutic regimen.

In the comparison between G1 and G2+G3, significant differences were observed in median blood serum eosinophils (360 *vs.* 530/mm3, p=0.047) and histologically severe disease (18.5% *vs.* 51%, p=0.003). No other significant differences were found, including age at symptom onset, time gap between symptom onset and diagnosis, personal history of allergic diseases, food sensitization, severe clinical disease, and serum total IgE levels (Table 1).

Discussion and conclusions

This study reflects our real-world experience in managing patients with EoE, highlighting the challenges in achieving symptom resolution and sustained endoscopic and histologic remission. This study included 130 patients diagnosed with EoE, both children and adults, of whom 79.2% were male (n=103), which is consistent with the recent literature. Male predominance may be explained by a genetically male predisposition to develop this disease[5,14,25].The mean time gap between the onset of symptoms and diagnosis was 49±65.7 months, in line with the 3-4 years described in previous studies[26]. The delay in diagnosis likely contributed to severe symptoms, including food impaction in 72.3% of patients. These factors may also account for the high proportion of patients (51.5%) with severe clinical disease and

over a third (42.3%) with severe histological disease at the time of diagnosis. These findings underscore the importance of early recognition and intervention to prevent disease progression and complications in patients with SLE.

Most patients (n=109; 83.8%) had atopic comorbidities, primarily allergic rhinitis (n=103; 79.2%) and asthma (n=34; 26.2%), supporting the concept that EoE may be part of the allergic march[25,27,28].

Laboratory data revealed a median serum total IgE of 164 KU/L (reference value of less than 100 KUA/L) and a peripheral eosinophilia of 476 cells/*µ*L (reference value of less than 300/µL), reflecting the role of Th2-driven inflammation in this condition[1,5,25].

Food sensitization was common (66.9%), particularly to nuts, milk, wheat, and eggs, in line with European EoE[7,13]. However, IgE-based and atopy patch testing are limited in guiding elimination diets, and current guidelines increasingly favor symptom-driven dietary interventions[10,29]. Despite this, allergy testing has been performed based on accumulated clinical experience[8,30].

The practical goals of EoE treatment are to prevent complications, stabilize the disease, and reverse fibrosis. Whether the last goal is achievable with current conventional treatments remains unclear[11]. Pharmacologic therapy consists of either PPIs and/or STC treatment. High doses of PPIs administered twice daily for 8 weeks are 40% to 60% effective in achieving histologic remission. The mechanism of PPI efficacy seems to be at least partly independent of acid suppression and may be due to its anti-inflammatory effects and restoration of esophageal barrier function. The efficacy of STC is 60% to 95%[13,31].

Food elimination diets are a treatment option for patients with EoE. A recent meta-analysis found that elemental diets were effective in 94.5% of cases, empiric elimination diets in 63.9-44.3%, and allergy test-directed diets in 39.5%[32]. Although elemental diets induce histologic remission in most patients, practical limitations restrict their use.

Additionally, a study found that allergy test-directed diets have lower remission rates but are more adhered to in clinical practice[33], with 64% of our patients following this approach.

The established treatment algorithm for more effective treatment includes regular evaluation of clinical, endoscopic, and histological responses to treatment. Most patients (79.2%) were on optimized therapy (PPI + STC ± elimination diet), but only 20.8% achieved a complete response (G1). In the group of patients who partially responded to treatment (G3), which included 64.6% of the patients, improvements in symptoms were observed in 34.5% of the patients. However, endoscopic and histological abnormalities persisted, with resolution seen in only 6.1% and 11.6% of patients, respectively.

Meanwhile, no significant differences in therapeutic options between responders and partial/non-responders were observed, highlighting the difficulty in achieving remission with optimized therapy.

Importantly, lower baseline peripheral eosinophil counts and less severe histological disease were associated with a complete response, suggesting distinct underlying pathogenic mechanisms (endotypes) and the potential value of these parameters as predictive biomarkers.

The emergence of dupilumab offers a promising option for patients unresponsive to conventional therapy[17,18,34,35]. We hope that in the near future, this treatment will become more accessible so that non-responders and partial responders to conventional treatment can benefit from it.

This study was limited by its retrospective design, variable treatment durations, and unequal group sizes. Nevertheless, it provides a comprehensive overview of EoE management and real-world treatment outcomes at a Portuguese tertiary center. Future studies should focus on validating minimally invasive biomarkers to predict treatment response, adopting standardized histologic scoring, and further elucidating the pathophysiology of EoE to guide personalized therapy.

In conclusion, early diagnosis, multidisciplinary care, and tailored treatment strategies are crucial for improving outcomes in EoE. Patients with lower eosinophil counts and milder histological disease are more likely to achieve complete remission with conventional therapies, emphasizing the need for predictive biomarkers and novel therapeutic approaches.

Author contributions: AGB and CC: conceptualization, formal analysis, writing – original draft. AGB, CC, MG: methodology, data curation, writing – review & editing.

Financial support: None.

Conflict of interest: The authors declare that there is no existence of economic or other types of conflicts of interest regarding the presented article.

Submitted: 01/06/2026. **Accepted:** 02/25/2026.

Chief-Editor: Ekaterini Goudouris.

Correspondence:
Ana Graça Bernardino
E-mail: anagracabernardino@gmail.com

References

1. Rossetti D, Isoldi S, Oliva S. Eosinophilic esophagitis: update on diagnosis and treatment in pediatric patients. Paediatr Drugs. 2020 Aug;22(4):343-56. https://doi.org/10.1007/s40272-020-00398-z. PMid:32519266.
2. Attwood SE, Smyrk TC, Demeester TR, Jones JB. Esophageal eosinophilia with dysphagia: a distinct clinicopathologic syndrome. Dig Dis Sci. 1993 Jan;38(1):109-16. https://doi.org/10.1007/BF01296781. PMid:8420741.
3. Kennedy KV, Muir AB, Ruffner MA. Pathophysiology of eosinophilic esophagitis. Immunol Allergy Clin North Am. 2024 May;44(2):119-28. https://doi.org/10.1016/j.iac.2023.12.001. PMid:38575212.
4. Straumann A, Spichtin HP, Bernoulli R, Loosli J, Vögtlin J. Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings. Schweiz Med Wochenschr. 1994 Aug 20;124(33):1419-29. PMid:7939509.
5. O'Shea KM, Aceves SS, Dellon ES, Gupta SK, Spergel JM, Furuta GT et al. Pathophysiology of eosinophilic esophagitis. Gastroenterology. 2018 Jan;154(2):333-45. https://doi.org/10.1053/j.gastro.2017.06.065. PMid:28757265.
6. Spergel JM, Brown-Whitehorn TF, Cianferoni A, Shuker M, Wang ML, Verma R et al. Identification of causative foods in children with eosinophilic esophagitis treated with an elimination diet. J Allergy Clin Immunol. 2012 Aug;130(2):461-467.e5. https://doi.org/10.1016/j.jaci.2012.05.021. PMid:22743304.
7. Vinit C, Dieme A, Courbage S, Dehaine C, Dufeu CM, Jacquemot S et al. Eosinophilic esophagitis: pathophysiology, diagnosis, and management. Arch Pediatr. 2019 Apr;26(3):182-90. https://doi.org/10.1016/j.arcped.2019.02.005. PMid:30827775.
8. Alves Marcelino JL, Cardoso de Aguiar R, Cabral Duarte F, Célia Costa A, Pereira-Barbosa MA. Pediatric eosinophilic esophagitis in Portugal. Eur Ann Allergy Clin Immunol. 2017 Mar;49(2):66-74. PMid:28294586.
9. Menard-Katcher C, Aceves S. Pathophysiology and clinical impact of esophageal remodeling and fibrosis in eosinophilic esophagitis. Immunol Allergy Clin North Am. 2024 May;44(2):129-43. https://doi.org/10.1016/j.iac.2023.12.002. PMid:38575213.
10. Dellon ES, Muir AB, Katzka DA, Shah SC, Sauer BG, Aceves SS et al. ACG clinical guideline: diagnosis and management of eosinophilic esophagitis. Am J Gastroenterol. 2025 Jan 1;120(1):31-59. https://doi.org/10.14309/ajg.0000000000003194. PMid:39745304.
11. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: proceedings of the AGREE Conference. Gastroenterology. 2018 Oct;155(4):1022-1033.e10. https://doi.org/10.1053/j.gastro.2018.07.009. PMid:30009819.
12. Hirano I, Chan ES, Rank MA, Sharaf RN, Stollman NH, Stukus DR et al. AGA institute and the joint task force on allergy-immunology practice parameters clinical guidelines for the management of eosinophilic esophagitis. Ann Allergy Asthma Immunol. 2020 May;124(5):416-23. https://doi.org/10.1016/j.anai.2020.03.020. PMid:32336462.
13. Gonsalves NP, Aceves SS. Diagnosis and treatment of eosinophilic esophagitis. J Allergy Clin Immunol. 2020 Jan;145(1):1-7. https://doi.org/10.1016/j.jaci.2019.11.011. PMid:31910983.
14. Carvalho S, Costa C, Marcelino J, Duarte FC, Barbosa MP. Esofagite eosinofílica numa consulta de alergia alimentar: caracterização e comparação entre idade pediátrica e idade adulta. Braz J Allergy Immunol. 2019;3(3):301-8. https://doi.org/10.5935/2526-5393.20190041.
15. 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 Aug;71(8):1459-87. https://doi.org/10.1136/gutjnl-2022-327326. PMid:35606089.
16. Kagalwalla AF, Wechsler JB, Amsden K, Schwartz S, Makhija M, Olive A et al. Efficacy of a 4-food elimination diet for children with eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2017 Nov;15(11):1698-1707.e7. https://doi.org/10.1016/j.cgh.2017.05.048. PMid:28603055.
17. 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. https://doi.org/10.1016/j.anai.2022.12.014. PMid:36521784.
18. European Medicines Agency. Summary of product characteristics: Dupixent [Internet]. Amsterdam: EMA; 2024 [cited 2024 Jul 15]. Available from: https://www.ema.europa.eu/pt/documents/product-information/dupixent-epar-product-information_pt.pdf.
19. Anyane-Yeboa A, Wang W, Kavitt RT. The role of allergy testing in eosinophilic esophagitis. Gastroenterol Hepatol. 2018 Aug;14(8):463-9. PMid:30302061.
20. Turjanmaa K, Darsow U, Niggemann B, Rancé F, Vanto T, Werfel T. EAACI/GA2LEN position paper: present status of the atopy patch test. Allergy. 2006 Dec;61(12):1377-84. https://doi.org/10.1111/j.1398-9995.2006.01136.x. PMid:17073865.
21. Furuta GT, Katzka DA. Eosinophilic esophagitis. N Engl J Med. 2015 Oct 22;373(17):1640-8. https://doi.org/10.1056/NEJMra1502863. PMid:26488694.
22. Gomez Torrijos E, Gonzalez-Mendiola R, Alvarado M, Avila R, Prieto-Garcia A, Valbuena T et al. Eosinophilic esophagitis: review and update. Front Med. 2018 Oct 9;5:247. https://doi.org/10.3389/fmed.2018.00247. PMid:30364207.
23. van Rhijn BD, Verheij J, Smout AJ, Bredenoord AJ. The Endoscopic Reference Score shows modest accuracy to predict histologic remission in adult patients with eosinophilic esophagitis. Neurogastroenterol Motil. 2016 Nov;28(11):1714-22. https://doi.org/10.1111/nmo.12872. PMid:27254480.
24. Dellon ES, Gupta SK. A conceptual approach to understanding treatment response in eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2019 Oct;17(11):2149-60. https://doi.org/10.1016/j.cgh.2019.01.030. PMid:30710696.
25. Navarro P, Arias Á, Arias-González L, Laserna-Mendieta EJ, Ruiz-Ponce M, Lucendo AJ. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. Aliment Pharmacol Ther. 2019 May;49(9):1116-25. https://doi.org/10.1111/apt.15231. PMid:30887555.
26. Castro Jiménez A, Gómez Torrijos E, García Rodríguez R, Feo Brito F, Borja Segade J, Galindo Bonilla PA et al. Demographic, clinical and allergological characteristics of Eosinophilic Esophagitis in a Spanish central region. Allergol Immunopathol. 2014 Sep-Oct;42(5):407-14. https://doi.org/10.1016/j.aller.2013.04.004. PMid:23845923.
27. Hill DA, Grundmeier RW, Ramos M, Spergel JM. Eosinophilic esophagitis is a late manifestation of the allergic march. J Allergy Clin Immunol Pract. 2018 Sep-Oct;6(5):1528-33. https://doi.org/10.1016/j.jaip.2018.05.010. PMid:29954692.
28. Ji R, Cui X, Zhi Y. Eosinophilic esophagitis and allergic susceptibility: a systematic review and meta-analysis. World Allergy Organ J. 2025 Apr 25;18(5):101054. https://doi.org/10.1016/j.waojou.2025.101054. PMid:40336814.

29. Eckmann JD, Ravi K, Katzka DA, Davis DR, See JA, Geno DR et al. Efficacy of atopy patch testing in directed dietary therapy of eosinophilic esophagitis: a pilot study. Dig Dis Sci. 2018 Mar;63(3):694-702. https://doi.org/10.1007/s10620-018-4928-4. PMid:29349695.

30. Esteves Caldeira L, Limão R, Brás R, Pedro E, Costa C. A real-world characterization of a cohort with eosinophilic esophagitis: looking for severity biomarkers. Eur Ann Allergy Clin Immunol. 2024 Mar 28;56(6):252-62. https://doi.org/10.23822/EurAnnACI.1764-1489.292. PMid:36975751.

31. Liacouras CA, Spergel JM, Ruchelli E, Verma R, Mascarenhas M, Semeao E et al. Eosinophilic esophagitis: a 10-year experience in 381 children. Clin Gastroenterol Hepatol. 2005 Dec;3(12):1198-206. https://doi.org/10.1016/S1542-3565(05)00885-2. PMid:16361045.

32. Arias A, Tejera-Muñoz A, Gutiérrez-Ramírez L, Molina-Infante J, Lucendo AJ. Efficacy of dietary therapy for eosinophilic esophagitis in children and adults: an updated systematic review and meta-analysis. Nutrients. 2024 Jul 11;16(14):2231. https://doi.org/10.3390/nu16142231. PMid:39064673.

33. 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. https://doi.org/10.1016/j.cgh.2023.01.019. PMid:36731591.

34. Dellon ES, Rothenberg ME, Collins MH, Hirano I, Chehade M, Bredenoord AJ et al. Dupilumab in adults and adolescents with eosinophilic esophagitis. N Engl J Med. 2022 Dec 22;387(25):2317-30. https://doi.org/10.1056/NEJMoa2205982. PMid:36546624.

35. Tripp CS, Cuff C, Campbell AL, Hendrickson BA, Voss J, Melim T et al. RPC4046, a novel anti-interleukin-13 antibody, blocks IL-13 binding to IL-13 α1 and α2 receptors: a randomized, double-blind, placebo-controlled, dose-escalation first-in-human Study. Adv Ther. 2017 Jun;34(6):1364-81. https://doi.org/10.1007/s12325-017-0525-8. PMid:28455782.