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# Eosinophilic Esophagitis: A Retrospective Analysis of Maintenance Therapy

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## ABSTRACT

**Objective:** Eosinophilic Esophagitis (EoE) is a chronic disease that can cause complications when left untreated. However, the actual guidelines do not clearly specify which category of patients would benefit the most from maintenance treatment. The objective of this study was to determine the rate of relapse in our population and to identify the demographic and clinical characteristics of those patients, so that we can establish a long-term strategy to target them.

**Methods:** This was a retrospective cohort study that included all adult patients who had a diagnosis of EoE between 2010 and 2020 at the Sherbrooke University Hospital Centre.

**Results:** 283 patients were included. Our population consists primarily of male (75.6%), young (63.8% under 45 years old) and atopic patients (67.7%). 37.8% had food impaction and 22.5% had a stenosis at diagnosis. In our center, the percentage of significant relapse is 18.4%. Individuals with a higher risk of relapsing were those with poor adherence to treatment (61.5% vs 38.5%; p-value=0.0) and with a more severe presentation of their disease such as esophageal stenosis (29.0% vs 16.0%; p=0.021) or bolus impaction (29.9% vs 11.4%; p=0.0).

**Conclusion:** A relapse rate as high as 18.4% in our population would justify maintenance treatment in most patients. However, our results show that a more severe presentation of the disease leads to more recurrences, so initiating maintenance treatment in this group should be a priority. Improving adherence to EoE treatment should also be a goal to achieve with our interventions.

**Keywords:** Esophageal eosinophilic; Therapy; Maintenance; Relapse; Oesophageal disease; Dysphagia; Remission; Oesophageal stenosis

## INTRODUCTION

With increasing incidence and prevalence, Eosinophilic Esophagitis (EoE) is a chronic disease that is considered the leading cause of dysphagia and food impaction. Over the last 30 years, the incidence increased from 0.35 to 9.45 cases per 100,000 person-years, with a prevalence estimated around 55 cases per 100 000 population [1]. If left untreated, inflammation can lead to strictures in half of patients after 10 years and 2/3 after 20 years [2]. This can result in incapacitating symptoms that affect patient quality of life. Before the 2017 "AGREE Conference," patients responding to an initial treatment with a Proton Pump Inhibitor (PPI) were placed in a different diagnostic category and often excluded from studies [3]. It is now well understood that the relation between Gastroesophageal Reflux Disease (GERD) and EoE is more complex, and they often coexist. Since that change in terminology, PPI can be considered as a treatment option in the same way as topical glucocorticoids and elimination diets. The 2020 guidelines developed jointly by the AGA (American Gastroenterology Association) and the JTF (Joint Task Force on Allergy-Immunology) describe those 3

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treatments as being effective, but do not specify if an option is better for certain categories of patients [4]. This vagueness in guidelines is linked to an important variability in the therapy prescribed by the gastroenterologists. Many experts agree on initiating a short-term treatment of 8 to 12 weeks for patients with active disease, but there is uncertainty as to what to do after this period. The chronic nature and the high rate of relapse of EoE would justify a maintenance treatment, but that conclusion is based on very few studies and there are no clear recommendations that guide us on which patients would benefit the most from this long-term treatment. The fact that some treatments, such as glucocorticoids, can result in complications when used for a long period also needs to be considered. The goal of our research was to establish whether patients who eventually develop significant relapses have some predictive characteristics. This would help us in selecting the group of patients who must start a maintenance therapy with priority.

# METHODS

## Study Population

We included all patients of 18 years and older who had a diagnosis of EoE in our hospital between 2010 and 2020. The diagnosis was made by biopsy with an Esophagogastroduodenoscopy (EGD) and the pathology needed to show at least 15 Eosinophils by High Power Field (HPF), which is in accordance with the usual definition [5]. We excluded paediatric patients and those with Eosinophilic infiltration in pathological results for other reasons than EoE (eg, GERD).

## Study Design and Recruitment

Our team conducted a retrospective cohort study, so recruitment was carried out by examining the medical records of the patients corresponding to our inclusion criteria. We investigated the CIRESS database, asking for all 18-years and older patients with a diagnosis of EoE at the "Centre Hospitalier Universitaire de Sherbrooke" (CHUS) between January 1 2010 and December 31 2020. We conducted research using the key words 'Eosinophilic Esophagitis' that could be observed as a diagnosis in the patient's file or in pathological results. We collected data (2010 to 2020) using the electronic platform 'ARIANE' after acceptance of our research protocol (2022-4530) in respect of ethics committee.

## Outcomes

The primary outcome of our study was to find out what is the percentage of significant relapse in the population of patients with a diagnosis of EoE. We defined a relapse as clinically significant if one of the following criteria was encountered during or after the use of a validated treatment for EoE:

1. Early histological (positive biopsy) or clinical (recurrence of initial symptoms) relapse in a period of 1 year, requiring a change/optimization of treatment or treating for a 2nd time.
2. 'Severe' relapse, at any moment, defined as one of the following:

- Emergency Department (ER) visit for food impaction or significant stenosis resulting in an emergency endoscopy or dilation.
- A state of malnutrition or inability to eat.

As a secondary objective, we wanted to identify the demographic and clinical characteristics of patients who tend to develop these relapses, so that we can eventually establish a long-term strategy targeting this group. Our other secondary outcome was to describe and analyze how gastroenterologists diagnose, treat and follow patients with EoE to eventually adopt a more standardized approach.

## Sample Size

Before starting the study, we established that a significant relapse rate greater than 15% in our population would be enough to justify maintaining treatment for most patients. We calculated the number of patients needed in our sample using a confidence interval of 95% and an error margin of 5%. This means that for a projected proportion of 15%, which varies from 10% to 20%, 196 patients were required to obtain a statistically significant population.

## Statistical Analyses

Demographic data are analyzed according to how the different variables are expressed. Dichotomic data are represented as a percentage with a confidence interval of 95% according to the Wilson method. The calculated mean and standard deviation are used for each continuous numeric variable of normal distribution. We established a confidence interval of 95% of the averages calculated using the normal approximation. The median and the values at the 5th and 75th percentile are used for the continuous numerical variables of non-normal distribution. To answer our primary outcome, which is the percentage of relapse, we present this result as a percentage with a confidence interval of 95% (Wilson method). Our 1st secondary outcome was to see if there are some predictive factors for relapses. For this, we performed univariate analyses using the Chi-square test for dichotomous and nonordinal categorical variables, Mantel-Haenszel test for ordinal variables, and Mann-Whitney test to compare the continuous variables between the 2 groups (with and without relapse).

# RESULTS

## Baseline Characteristics

283 patients were included. **Table 1** presents the baseline characteristics of our population. Our sample consists primarily of male (75.6%), young (63.8% under 45 years of age), and atopic patients (67.7%). At diagnosis, 37.8% of the patients presented food impaction in the ER and 22.5% had stenosis at the initial EGD.

**Table 1:** Patients baseline characteristics

| Demographic characteristics | Total: N (%) |
|---|---|
| **Sex** | |
| Men | 214/283 (75.6%) |
| **Age of diagnosis** | |
| Mean | 39.8 (± 13.3) |

| | |
|---|---|
| 18 years-29 years old | 73/282 (25.9%) |
| 30 years-44 years old | 107/282 (37.9%) |
| 45 years old and older | 102/282 (36.2%) |
| Smoking (previous or active) | 42/258 (16.3%) |
| Atopy | 178/263 (67.7%) |
| Allergic rhinitis | 122/176 (69.3%) |
| Asthma | 85/176 (48.3%) |
| Food allergy | 54/176 (30.7%) |
| Atopic dermatitis | 21/176 (11.9%) |
| **Autoimmune disease and other medical conditions** | |
| Inflammatory bowel disease | 9/283 (3.2%) |
| Rheumatoid arthritis or spondyloarthropathies | 8/283 (2.8%) |
| Psoriasis | 5/283 (1.8%) |
| Coeliac disease | 4/283 (1.4%) |
| Concomitant eosinophilic gastroenteritis | 3/283 (1.0%) |
| Before bariatric surgery | 3/283 (1.0%) |
| Repetitive pericarditis | 2/283 (0.7%) |
| HIV | 2/283 (0.7%) |
| Cystic fibrosis | 2/283 (0.7%) |
| **Clinical characteristics** | |
| Dysphagia | 254/281 (90.4%) |
| Food Impaction | 146/281 (52.0%) |
| ER consultation with food impaction at the moment of diagnosis | 107/283 (37.8%) |
| GERD/pyrosis | 61/281 (21.7%) |
| Dyspepsia or thoracic pain | 14/283 (4.9%) |
| Esophageal laceration or perforation | 4/283 (1.4%) |
| Asymptomatic | 3/283 (1.1%) |
| Non-adherence | 96/274 (35.0%) |
| 18 years-29 years old | 39/71 (54.9%) |
| 30 years-44 years old | 37/106 (34.9%) |
| 45 years and older | 19/96 (19.8%) |
| **Initial endoscopic findings** | |
| Abnormal macroscopic appearance at endoscopy | 256/283 (90.5%) |
| Trachealization, rings or furrows | 237/273 (86.8%) |
| Strictures, narrow caliber esophagus, or stenosis | 62/275 (22.5%) |
| Exudates, white spots or oedema | 34/273 (12.5%) |
| Normal macroscopic appearance at endoscopy | 27/283 (9.5%) |
| **Initial histologic findings** | |
| Number of eosinophils in proximal esophagus biopsy | |
| <50 per HPF | 162/245 (66.1%) |
| ≥ 50 per HPF | 83/245 (33.9%) |

## Primary Outcome

In **Table 2**, the results of our primary outcome are exposed. We encountered 28 early (11.2%) and 37 severe (14.7%) relapses for a cumulative significant relapse percentage of 18.4%. The severe relapses are made up entirely of patients who presented with bolus impaction.

**Table 2:** Relapse (primary outcome)

| Variables | N (%) | Confidence interval |
|---|---|---|
| Early relapse | 28/250 (11.2 %) | 7.8-15.6 |
| Severe relapse | 37/252 (14.7 %) | 10.8-19.6 |
| Significant relapse | 52/283 (18.4 %) | 14.3-23.3 |
| Relapse subanalyses | | |
| Clinical relapse when treatment stopped | 74/108 (68.5 %) | 59.2-76.5 |
| Persistence of clinical symptoms with maintenance treatment | 74/233 (31.8 %) | 26.1-38.0 |
| Clinic or histological relapse with maintenance treatment | 37/226 (16.4 %) | 12.1-21.7 |
| Persistence of positive histology with maintenance treatment | 131/170 (77.1 %) | 70.2-82.7 |
| Persistence of positive histology or clinical symptoms with maintenance treatment | 146/186 (78.5 %) | 72.0-83.8 |

## Secondary Outcomes

Characteristics associated with relapses and remissions: Table 3 illustrates the characteristics of patients who developed significant relapse. No major statistical association arises between relapses and demographic characteristics, but we can still observe a tendency of a little more men (80.8% vs 74.5%), atopic patients (71.2% vs 66.8%), and young patients 18 to 29 years old (35.5% vs. 23.8%). As shown in **Figure 1**, the patients who initially had a food impaction (29.9% vs 11.4%; p-value=0.0) or Esophageal Stenosis (29.0 vs 16.0%; p-value=0.021) at the time of diagnosis were significantly more at risk of developing a relapse over time. Furthermore, subjects identified as non-adherent represented 35.0% of our entire population, but up to 61.5% of patients with a significant relapse. A younger age was associated with poorer adherence to treatment. The sample of patients with a significant relapse had received more dilations and steroids, as we can understand that they probably have a more severe disease. Finally, in **Figure 2**, we show the mean interval between the beginning of symptoms and the moment of diagnosis, which are 6.49 years in the group with relapse and 4.52 years in the other group.

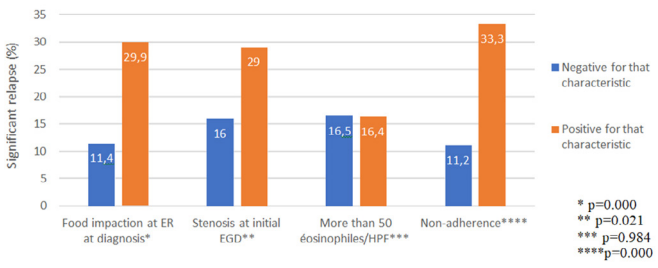


**Figure 1:** Percentage of relapse by severity markers

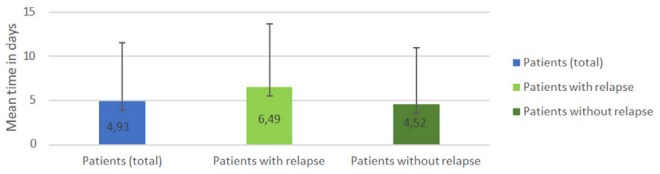


**Figure 2:** Mean time interval between beginning of symptoms and diagnosis

**Table 3** also describes the characteristics of the patients who achieved a state of remission after the 1st line of treatment. Among them, there were few young patients (only 16.3% between 18 and 29 years) and mainly compliant patients (76.7% vs 23.3; p-value=0.089). More remissions were obtained in patients who received a combination of treatments at the beginning (23.3% vs 13.1%; p-value=0.042).

## Management of Eoe

In **Tables 4 and 5**, we present data that describe how EoE is managed at our center. For all lines of treatment, PPI was the most popular, regardless of the year of diagnosis. 98.9% of patients received a PPI at some point. In most patients (97.3%), a maintenance regimen was introduced, but included PPI-only treatments that represented up to 71.7% of 1st line therapies. Another treatment modality, such as steroids or diet, was often added as a combination in the 2nd or 3rd line of treatment, but in total 73.5% of the patients had only one line of treatment during our study. Although we observed an improvement over the years, only 31.7% of biopsies were adequately completed and 63.0% of control endoscopy was performed. 4 patients had a significant adverse reaction due to their treatment, all of which were a form of candida infection.

**Table 3:** Characteristics of patients among those with significant relapse and remission

| Variables | Significant relapse n (%) | P value | Histologic remission in 1st line n (%) | <50 per HPF |
|---|---|---|---|---|
| | | **Demographics** | | |
| | | **Sex** | | |
| Men | 42/52 (80.8 %) | 0.3 | 32/43 (74.4 %) | 0.778 |
| Women | 10/52 (19.2 %) | 0 | 11/43 (25.6 %) | 0 |
| Smoker | 4/51 (7.8 %) | 0.1 | 11/42 (26.2 %) | 0.067 |
| Non-smoker | 47/51 (92.2 %) | | 31/42 (73.8 %) | |
| Atopy | 37/52 (71.2 %) | 0.6 | 28/43 (65.1 %) | 0.721 |
| No atopy | 15/52 (28.8 %) | | 15/43 (34.9 %) | |
| | | **Age of diagnosis** | | |
| 18 years-29 years old | 18/51 (35.3%) | | 7/43 (16.3 %) | |
| 30 years-44 years old | 17/51 (33.3 %) | 0.152a | 17/43 (39.5 %) | 0.092a |
| 45 years and older | 16/51 (31.4 %) | | 19/43 (44.2 %) | |
| | | **Treatments received or not** | | |
| PPI | 52/52 (100 %) | 0.4 | 43/43 (100 %) | 0.382 |
| No PPI | 0/52 (0 %) | | 0/43 (0 %) | |
| PPI alone | 18/52 (34.6 %) | 0 | 26/43 (60.5 %) | 0.078 |
| No PPI-only | 34/52 (65.4 %) | | 17/43 (39.5 %) | |
| Glucocorticoids (total) | 32 /52 (61.5 %) | 0 | 18/43 (41.9 %) | 0.497 |
| No glucocorticoids | 20/52 (38.5 %) | | 25/43 (58.1 %) | |
| Fluticasone | 27/52 (51.9 %) | 0 | 10 (23.3 %) | 0.264 |
| No Fluticasone | 25/52 (48.1 %) | | 33 (76.7 %) | |
| Budesonide | 16/52 (30.8 %) | 0 | 5 (11.6 %) | 0.152 |
| No budesonide | 36/52 (69.2 %) | | 38 (88.4 %) | |
| Endoscopic dilation | 8/52 (15.4 %) | 0 | 3 (7.0 %) | 0.466 |
| No endoscopic dilation | 44/52 (84.6 %) | | 40 (93.0 %) | |
| Elimination diet | 9/52 (17.3 %) | 0.1 | 2 (4.7 %) | 0.961 |
| No elimination diet | 43/52 (82.7 %) | | 41 (95.3 %) | |
| Combination of treatment | 34/52 (65.4 %) | 0 | 17 (39.5 %) | 0.042 |
| No combination of treatment | 18/52 (34.6%) | | 26 (60.5 %) | |

**Table 4:** Mangement description data by year of diagnosis

| Variables | Year of diagnosis 2010-2012 N (%) | Year of diagnosis 2013-2017 N (%) | Year of diagnosis 2018-2020 N (%) | All years combined N (%) | P value Pearson Chi-square | P-value of linear-by-linear association |
|---|---|---|---|---|---|---|
| | | | **Diagnosis and follow-up data** | | | |
| Biopsy following recommandations | 13/60 (21.7 %) | 49/144 (34.0 %) | 27/77 (35.1 %) | 89/281 (31.7 %) | 0.169 | 0.113 |
| Control EGD proposed | 34/60 (56.7 %) | 92/145 (63.4 %) | 51/76 (67.1 %) | 177/281 (63.0 %) | 0.451 | 0.218 |
| Allergoloy consult | 20/60 (33.3 %) | 38/142 (26.8 %) | 20/76 (26.3 %) | 78/278 (28.1 %) | 0.589 | 0.391 |
| | | | **Treatments data** | | | |
| PPI | 58/59 (98.3 %) | 134/136 (98.5 %) | 75/76 (98.7 %) | 267/271 (98.5 %) | 0.984 | 0.858 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Fluticasone | 22/59 (37.3 %) | 18/136 (38.3 %) | 7/76 (9.2 %) | 47/271 (17.3 %) | 0 | 0 |
| Budesonide | 2/59 (3.4 %) | 6/136 (4.4 %) | 10/76 (13.2 %) | 18/271 (6.6 %) | 0.026 | 0.017 |
| Diet | 3/59 (5.1 %) | 8/136 (5.9 %) | 2/76 (2.6 %) | 13/271 (4.8 %) | 0.565 | 0.464 |
| Dilation | 2/59 (3.4 %) | 8/136 (5.9 %) | 3/76 (3.9 %) | 13/271 (4.8 %) | 0.695 | 0.941 |
| Combination | 25/59 (42.4 %) | 32/136 (23.5 %) | 16/76 (21.1 %) | 0 | 0.01 | 0.008 |

**Table 5:** Mangement description data byline of treatment

| Variables | 1st line of treatment n (%) | 2nd line of treatment n (%) | 3rd line of treatment n (%) | All line of treatment combined n (%) |
|---|---|---|---|---|
| **Description of the line of treatment used and prescribed** | | | | |
| PPI | 268/272 (98.5 %) | 63/73 (86.3 %) | 16/19 (84.2 %) | 269/272 (98.9 %) |
| PPI-alone | 195/272 (71.7 %) | 14/73 (19.2 %) | 1/19 (5.3 %) | 155/272 (57.0 %) |
| Glucocorticoid (total) | 61/272 (22.4 %) | 49/73 (67.1 %) | 11/19 (57.9 %) | 101/272 (37.1 %) |
| Fluticasone | 47/272 (17.3 %) | 28/73 (38.4 %) | 4/19 (21.1 %) | 76/272 (27.9 %) |
| Budesonide or Jorveza | 18/272 (6.6 %) | 24/73 (32.9 %) | 8/19 (42.1 %) | 44/272 (16.2 %) |
| Diet (total) | 13/272 (4.8 %) | 17/73 (23.3 %) | 7/19 (36.8 %) | 31/30 (11.4 %) |
| 6-food elimination diet | 0 | 0 | 0 | 5/30 (16.7%) |
| 4-food elimination diet | 0 | 0 | 0 | 1/30 (3.3 %) |
| 2-food elimination diet | 0 | 0 | 0 | 2/30 (6.7 %) |
| 1-food elimination diet | 0 | 0 | 0 | 12/30 (40.0 %) |
| Allergy testing targeted diet | 0 | 0 | 0 | 8/30 (26.7 %) |
| Elementary diet | 0 | 0 | 0 | 0 |
| Endoscopic dilation | 13/272 (4.8 %) | 6/73 (8.2 %) | 7/19 (36.8 %) | 23/272 (8.5 %) |
| Others (Montelukast, chromoglycate) | 0 | 3/73 (4.1 %) | 2/19 (10.5 %) | 5/272 (1.8 %) |
| Number of patients who stopped at this line of treatment | 208/283 (73.5 %) | 56/283 (19.8 %) | 19/283 (6.7 %) | 0 |
| **Treatment combinations** | | | | |
| Combinations (total) | 73/272 (26.8 %) | 52/73 (71.2 %) | 16/19 (84.2 %) | 108/272 (39.7 %) |
| **Treatments used as combination** | | | | |
| **PPI** | | | | |
| Fluticasone | 73/73 (100 %) | 49/52 (94.2 %) | 15/16 (93.8 %) | 0 |
| Budesonide | 47/73 (64.4 %) | 27/52 (51.9 %) | 4/16 (25.0 %) | 0 |
| Endoscopic dilation | 18/73 (24.7 %) | 21/52 (40.4 %) | 7/16 (43.8 %) | 0 |
| Diet | 13/73 (17.8 %) | 6/52 (11.5 %) | 7/16 (43.8 %) | 0 |
| | 11/73 (15.1 %) | 14/52 (26.9 %) | 6/16 (37.5%) | 0 |
| **Maintenance treatment** | | | | |
| Patients started on maintenance treatment | 0 | 0 | 0 | 254/261 (97.3 %) |

## DISCUSSION

The main objective of our study was to evaluate the relapse rate of Esophageal Eosinophilic and to see if some groups were at greater risk. In our hospital, the percentage of relapse is 18.4%, a number we consider high enough to propose maintenance treatment to most patients. Within the patients receiving maintenance treatment, clinical symptoms were well controlled in 68.2% of them. In the opposite, 68.5% of the patients had a recurrence of symptoms when treatment was stopped. This is consistent with many anterior studies showing a high relapse rate, like the one by Dellon ES, et al. that concluded with 57% of relapses in their population of 58 patients in a period of less than a year. In a retrospective study of Greuter T, et al. 82% of patients had a clinical recurrence after discontinuation of treatment, allowing only 1.7% of the entire cohort of patients to stop long-term therapy [6-8]. In a study of Straumman A, et al. only 20.6% of subjects receiving a placebo were in clinical remission after 48 weeks with 89.7% who had a proven histological relapse [9]. This study also demonstrates the relevance of maintenance treatment by obtaining a remission rate of approximately 75% in patients receiving orodispersible budesonide treatment vs 4.4% with placebo. Our percentages of clinical remission and relapse are similar to those we can find out reading the literature on the subject. However, our histological and total relapse rate is lower than in some of the studies discussed and presented above. This could be explained by the fact that histology was never completely normalized in 77.1% of the patients in our study, making it harder to identify histologic relapses later on. We believe that this high percentage of patients with a biopsy that remained positive can be attributed to many patients never having

a treatment modification for different reasons (EGD never repeated, histology stays positive, but the patient feels well clinically, so the treatment was kept the same, nonadherence or lost at follow-up, patient discharged after starting a PPI, etc.). In conclusion, in many patients, the treatment could have been optimized because most patients (73.5%) only received one line and often only a PPI-only therapy. Our study reveals that patients, especially those with a more severe initial presentation, are at greater risk of relapsing. Maintenance treatment should be used prioritizing patients with esophageal stenosis or food impaction at the time of diagnosis because they significantly develop more relapses. Young people are also a population of patients that could be targeted considering that their relapse rate also seemed to be higher and obtaining a fast histological state of remission was more difficult. This could potentially be explained by the fact that the rate of nonadherence is significantly higher in this group. A study of 177 patients published in 2022 which specifically addresses the subject of nonadherence to the treatment of EoE, obtained a rate of nonadherence of 41.8% in their study population, similar to our result of 35.0% [10]. An interesting finding is that many factors (young age, more severe symptoms, longer duration of the disease) that the authors identified as being related to poor adherence to treatment are also associated with more relapses in our study. Since non-compliance was associated with more severe and significant relapses in our study, this is another argument that justifies the relevance of long-term maintenance treatment.

With the inclusion of 283 patients, our sample was statistically significant. When we compare the demographics and clinical characteristics of our population with the data encountered in anterior studies, we notice that they are very similar: 75.6% of men (vs 75%), 67.7% atopic patients (vs 75%), 52.0% food impactions (vs 54.0%), 9.5% with visually normal endoscopy (vs 10%) and a mean interval between the beginning of symptoms and diagnosis of 4.93 years vs 4.5 years [11]. If we focus on that last result, we can recall that in the group with a significant relapse, the interval was longer (6.49 years). It is possible to understand that diagnosing and starting a treatment early is necessary to avoid remodeling of esophageal tissue caused by prolonged inflammation.

The most popular treatment prescribed as the 1st line by gastroenterologists was PPI (71.7%), followed by glucocorticoids (22.4%) and diet (4.8%). Most of the patients (40.0%) had one food removed from their diet. These results are consistent with a study of 589 patients by Laserna-Mendieta and al proving that PPI was the 1st choice of treatment in 76.4% compared to 10.5% of steroids and 7.8% of diets [12]. However, the most effective option to induce both clinical and histological remission was topical glucocorticoids (67.7%), followed by elimination diets (52.0%) and PPI (50.2%). This study is interesting because it shows that PPI, which is the most popular therapy, is not the best way to obtain a state of remission. Our study also indicates that using a combination of treatments earlier was more likely to lead to remission. PPI can precipitate a recovery in clinical symptoms, but that can lead to a false sense of control of disease. Indeed, some studies such as the one by Safroneeva and al suggest that an improvement in symptomatology is not a good predictor of the endoscopic and histological remission of the disease. This may justify the need for close follow-up by control gastroscopy [13]. In our study, maintenance treatment was introduced in 97.3% of patients, which was more than expected. However, there is still some work to do because it was often a PPI-only treatment, and long-term follow-up and management could have been improved in many patients. In our healthcare center, although we observed an improvement over the years, only 31.7% of biopsy was performed according to the recommendations and 63.0% of the EGD control was proposed. Among patients receiving maintenance treatment, 4 had candida infection (1.6%), a lower number than observed in previous studies that reported 8.7% candida esophagitis in patients taking steroids.

Among the strengths of our study, we were able to obtain a statistically significant population. Because demographics and clinical characteristics are very similar to those found in the literature and references, our sample of patients was representative of reality. Our population is also definitely complete, since patients with EoE are required to undergo an endoscopy to obtain a diagnosis, and our research included every available pathological result. The objective of our study is relevant because it answers the need to clarify and standardize the management of the disease. The results obtained are interesting and statistically significant in identifying some groups of patients at high risk of developing relapse of the disease. Our study also has some limitations. Due to its retrospective nature, there were some missing data in the patient's medical file, for example, some poorly detailed endoscopic reports or undocumented information. With many non-adherent patients or lost at follow-up, it was more difficult to assess the direct effectiveness of the different treatment options for EoE. Many combinations of treatments overlapped, making it more difficult to clearly identify what the 1st, 2nd, and 3rd lines were. For that reason, we did some nonexclusive statistical analyses (PPI vs no PPI, steroid vs no steroid received, etc.). Some data collected, such as clinical response and remission, were more subjective, so we focused our study on more objective results, such as histopathology. However, because many patients remained with significant positive Eosinophilic Infiltration, the number of histological relapses could have been underestimated. Furthermore, it is possible to miss the capture of some relapses because the duration of follow-up was too short, for example, for patients recruited in the last couple of years [14]. Our results are still valid because, as demonstrated in previous studies, clinically most relapses occurred over a period of less than 1 year; therefore, most relapses should have been identified.

## CONCLUSION

To conclude, with a high recurrence rate of 18.4%, our results support other previous studies that recommend, with increasing evidence, maintenance treatment for most patients with EoE. However, our findings show that it is mainly patients with a more severe initial presentation of their disease that should be treated with priority. To improve adherence to treatment, it is important to explain to patients with a diagnosis of EoE the chronic nature of their disease and the importance of taking a long-term maintenance treatment. Further studies on the acceptance of the different treatment options would

be interesting. Finally, with our work we recognized groups of patients at risk of relapses and that could help to complement and put into practice a severity index like the one published in an article by Dellon and al in July 2022. A clinical score like this could help categorize and target patients with a higher probability of developing complications, but prospective studies would be necessary in the future.

## SUMMARY OF AUTHOR CONTRIBUTIONS

- Main author: Luca De Rico
- Authors: Mandy Malick, Marie-Pier Bachand
- We confirm that each individual named as an author meets the uniform requirements of the journal criteria for authorship.

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## DATA AVAILABILITY STATEMENT

The datasets analyzed during the current study are partially in the manuscript. The complete datasets are available on demand.

## CONFLICT OF INTEREST

None.

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