ORIGINAL ARTICLE

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Baseline Peripheral Eosinophil Count Independently Predicts Proton Pump Inhibitor Response in Eosinophilic Esophagitis

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ABSTRACT

In eosinophilic esophagitis (EoE), to evaluate the predictive usefulness of baseline peripheral absolute eosinophil counts (AECs) for the proton pump inhibitor (PPI) response.

Context : In around 50% of EoE patients, PPI results in histologic remission; nevertheless, there are rarely clinically significant differences.
Examine : An adult EoE patient cohort from a tertiary facility between 2012 and 2016 is the subject of this retrospective cohort study. After undergoing twice-daily PPI trials for at least eight weeks, all patients had additional esophageal biopsies, and their histologic response (less than 15 eosinophils/high power field) determined whether they should be classified as PPI-r-EoE or PPI-nr-EoE. Prior to the index endoscopy, baseline peripheral AEC was acquired within a month. Fisher exact/Student t test (univariate) and logistic regression (multivariable) were used for the analyses. Fisher exact/Student t test (univariate) and logistic regression (multivariable) were used for the analyses.
Conclusions : In EoE patients, baseline peripheral eosinophilia independently predicts food impaction and PPI nonresponse. Auxiliary.

Keywords
eosinophilic esophagitis, eosinophil, eosinophilia, proton pump inhibitor, food impaction

INTRODUCTION

A chronic inflammatory illness of the esophagus, eosinophilic esophagitis (EoE) is thought to be caused by exposure to environmental and food allergens. It is the most common cause of dysphagia and food impaction in children and young adults, and it is observed in 2% to 7% of patients undergoing upper endoscopy for any reason.1. Proton pump inhibitors (PPIs), elimination diets, and topical steroid therapy are the current treatments for EOE. It was formerly believed that PPI-responsive esophageal dysphagia (PPI-r-EoE) was a distinct condition from EoE. Nevertheless, it has been discovered that these individuals are identical to PPI nonresponsive esophageal dysphagia (PPI-nr-EoE) patients in terms of clinical, endoscopic, and histological characteristics.2. PPI-r-EoE patients are now regarded as a subset of EoE patients, in accordance with the most recent consensus standards.3.

Finding PPI response predictors could enable early tailored treatment for EoE. Given that the length of untreated disease is associated with unfavorable outcomes such food impactions and fractured bones, this could lead to a shorter time to disease remission, fewer endoscopies required, and possibly a decreased incidence of EoE-related consequences.5. About 50% of EoE6 patients have peripheral eosinophilia, which has been studied as a noninvasive indicator of inflammatory activity in esophageal patients chosen for PPI therapy.
Therefore, our goal was to contrast PPI-TABLE 1's baseline pretreatment peripheral AEC.

RESOURCES AND TECHNIQUES

Examine the Population

Retrospective cohort analysis conducted from May 2012 to September 2016 on EoE patients at two tertiary hospitals: Brigham and Women's Hospital and Faulkner Hospital. At the time of the index upper endoscopy, all of the included EoE patients reported having esophageal symptoms and had ≥ 15 eosinophils/high power field (hpf) on esophageal mucosal biopsies. Following an index endoscopy, all patients were given twice-daily PPI for at least eight weeks. A follow-up endoscopy was then performed to collect repeat biopsies to assess a histologic response. The study excluded patients having a history of significant esophageal motility issue, prior foregut surgery, or gastrointestinal (GI) cancer.

Data Gathering and Results

Electronic medical records contained information on the patient's demographics, allergy history, endoscopic indications

and findings, and laboratory and pathology reports. The highest number of eosinophils per hpf found in any esophagus biopsy sample under light microscopy was used to calculate the peak esophageal eosinophil density. Prior to the start of the PPI experiment, baseline peripheral AEC was measured within a month of the index endoscopy. Within a month following the index endoscopy, patients without peripheral AEC-containing laboratory results were not included in the study. The main result of PPI was a histologic reaction. PPI-r-EoE patients had esophageal biopsy results from post-PPI trial endoscopy with <15 eosinophils/hpf, while PPI-nr-EoE patients had persistent eosinophilia (≥ 15 eosinophils/hpf) (Fig. 1). The following were secondary outcomes: food impaction, allergy history.

Schema of the EoE patients included in Figure 1. When esophageal mucosa samples were performed during index upper endoscopy for esophageal symptoms, all included patients had > 15 eosinophils/hpf. Counts of peripheral eosinophils were taken at the time of the index upper endoscope. Every patient had a repeat upper endoscopy after starting twice-daily PPI medication for at least eight weeks. During follow-up endoscopy, esophageal biopsies from individuals with PPI-nr-EoE showed persistent eosinophilia (≥ 15 eosinophils/hpf), while those with PPI-r-EoE showed <15 eosinophils/hpf. PPI stands for proton pump inhibitor; PPI-nr-EoE denotes PPI non-responsive EoE; PPI-r-EoE denotes PPI responsive EoE. EoE stands for eosinophilic esophagitis.

Analyses StatisticalThe SAS 9.3 statistical program (SAS Institute Inc.) was used for all statistical analyses. To evaluate the differences, the Student t test for continuous variables and the Fisher exact test for binary variables were used.

SAS Institute Inc. statistics package. The PPI-nr-EoE and PPI-r-EoE cohorts were compared using the Student t test for continuous variables and the Fisher exact test for binary variables. In order to determine whether baseline peripheral AEC independently predicts PPI response, multivariable analyses were performed using logistic regression, controlling for potential confounders such as sex, age, body mass index (BMI), peak esophageal eosinophil density on index endoscopy, history of allergies, and tobacco use.

prevalence of higher than 0.5 K/μL baseline peripheral AEC. Individuals who had a history of food impaction, a diagnosis made in the winter, or PPI-nr-EoE were significantly more likely to have elevated peripheral AEC at baseline. PPI-nr-EoE, PPI nonresponsive EoE; PPI-r-EoE, PPI responsive EoE; AEC, absolute eosinophil count. In EoE patients, eosinophilia at baseline continued to be independently correlated with nonresponse to PPI.

Numerous inflammatory diseases have been studied in relation to peripheral eosinophilia. Peripheral eosinophilia has been linked to more severe and poorly controlled illness in patients with asthma, a common concomitant condition in patients with EoE.11 Additionally, a relationship has been noted between peripheral eosinophilia and heightened severity in several inflammatory gastrointestinal disorders. Peripheral eosinophilia increases the risk of pediatric onset and more severe inflammatory bowel disease in patients with inflammatory bowel disease.12 Peripheral eosinophilia is associated with a higher frequency of concomitant atopy and more extensive GI involvement in patients with non-esophageal eosinophilic GI illness of the stomach and colon. Thirteen Previous research on EoE has revealed that peripheral AEC may, with 75% sensitivity and 87% specificity,14 separate EoE patients from controls,15 reflect eosinophilic density on esophageal biopsies,7,8,14–16 aid in tracking the efficacy of topical steroids as a treatment, and elimination diets,7,9 and forecast the occurrence of symptoms related to dysphagia.10 But most of these studies did not include patients who responded to PPI therapy; this was mainly because PPI-responsive disease was not previously included in most research and was thought of as a distinct disease entity rather than a subset of EoE.

The exact mechanism by which PPI causes a histologic response in people with endometriosis has not been completely determined and could involve multiple factors. While acid suppression may lessen the likelihood that acid reflux or other triggers would cause esophageal eosinophilia.

RESULTS

During the course of the trial, 247 patients were found to have EoE. Out of them, 183 were found to be eligible for inclusion; they had peripheral AEC collected at baseline, within a month of the index endoscopy, and repeat endoscopy and biopsies performed at least eight weeks following the start of the PPI experiment. Of the individuals who were included, 92 (50.3%) showed a histologic response to PPI, whereas 91 continued to have eosinophilia. The features of the two patient groups are contrasted in Table 1. PPI-r-EoE and PPI-nr-EoE patients did not significantly differ in terms of age, sex, race/ethnicity, BMI, median peak esophageal eosinophil density on index endoscopy, smoking, or allergy history overall.

Comparisons of Peripheral Absolute Eosinophil Counts: Univariate Analysis

Subjects with PPI-nr-EoE had significantly higher baseline peripheral AEC than those with0.41 ± 0.59 vs 0.24 ± 0.16 K/μL, P = 0.013) for PPI-r-EoE. For second As secondary results, baseline peripheral AEC did not significantly differ between those with and without a history of allergies (0.35 ± 0.53 vs 0.28 ± 0.20 K/μL, P = 0.34) or between individuals with and without a history of food impaction (0.34 ± 0.22 vs 0.33 ± 0.52 K/μL, P = 0.87). Additionally, there were no statistically

significant variations in the baseline peripheral AEC between the seasons that had index endoscopy performed (spring: 0.30 ± 0.29 vs summer: 0.27 ± 0.21 vs fall: 0.25 ± 0.16 vs winter: 0.49 ± 0.80 K/μL). When the peripheral AEC was dichotomized, higher baseline AEC (> 0.5 K/μL) was linked to a higher or microscopic, potentially due to underlying reflux, increasing the possibility that immune cells will be exposed to ingested allergens.

Peripheral AEC may be used to guide treatment for patients with asthma, including assessing eligibility for anti-interleukin therapy20 and forecasting response to anti-IgE medications.21 Therefore, knowledge regarding peripheral AEC may aid in customizing the treatment of asthma that is resistant to steroid-based medications. Our results might also bolster a comparable function for peripheral AEC in directing the selection of EoE treatment. For EoE patients without peripheral eosinophilia, for instance, a PPI trial might be a more sensible starting therapy. In contrast, individuals with baseline increased peripheral AEC might be more likely to fail PPI and benefit from topical steroids or elimination diets (Fig. 3). Furthermore, as peripheral AEC has been linked to food impaction, it may help identify individuals and act as a predictor for an increased risk of fracture.

CONCLUSIONS

Peripheral AEC was demonstrated to be an independent predictor of the histologic response to PPI medication in EoE patients. Furthermore, there was a strong correlation found between peripheral eosinophilia and a history of food impaction. Peripheral AEC may be useful in individualized treatment for EoE patients at the time of diagnosis, with a cutoff of > 0.5 K/μL. This could minimize the duration of illness remission and lower the risk of sequelae. To validate the use of peripheral AEC in monitoring disease activity for patients with end-of-life issues, predicting response to medication, and customizing a therapeutic approach for each patient, further prospective trials are required.

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