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Prolonged Time to Diagnosis of Eosinophilic Esophagitis Despite Increasing Knowledge of the Disease

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dysphagia; corticosteroids; symptom response

Introduction

Eosinophilic esophagitis (EoE) is a chronic condition characterized by eosinophilic-predominant inflammation and esophageal dysfunction.^{1,2} EoE represents a rapidly increasing cause of morbidity and a growing health problem.

Prior to the 1990s, clinicians infrequently recognized EoE. However, the publication of three seminal papers in the mid-1990s, triggered a rapid increase in publications, facilitated development of guidelines,^{1,2} and increased recognition of EoE. Whether this substantial increase in the medical literature translated into a more expedient diagnosis remains unknown. This study aimed to assess whether the symptomatic period preceding the diagnosis of EoE has decreased over time.

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Dellon: Project conception; supervision; data analysis/interpretation; manuscript drafting; critical revision.

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Methods

We conducted a retrospective cohort study utilizing the University of North Carolina (UNC) EoE Clinicopathologic Database between 2000 and 2014. The UNC IRB approved this study. This database contains data extracted from medical records for incident cases of EoE at UNC, diagnosed per consensus guidelines, with exclusion of PPI-REE.^{1,2} The outcome variable was length of symptoms preceding diagnosis and the independent variable was year of diagnosis. Potential confounders included gender, race, age at diagnosis, dysphagia, history of food impaction, symptoms of abdominal pain, chest pain, and heartburn, and concomitant atopic diseases.

A linear regression model was constructed to assess the unadjusted relationship between year of diagnosis and symptom length, then analysis of covariance assessed the relationship after adjusting for covariates. We calculated the predicted length of undiagnosed symptomatic periods for years corresponding with the publication of management guidelines: 2000 – 2006 (before first guidelines), 2007 – 2011 (after first guidelines), and after 2011 (after second guidelines).^{1,2} Additional adjusted models were constructed after stratifying by child (<18 years) or adult (≥ 18 years) status. All analyses were performed using Stata 14.1 (College Station, TX). The supplementary materials contain full methodological details.

Results

A total of 677 EoE cases were included in this study. At diagnosis, the mean age was 26 years (range 1–82), 69% were male, 81% were white and 40% had a history of an atopic condition. Dysphagia, heartburn, abdominal pain, and chest pain were reported in 71%, 39%, 22%, and 11% of patients, respectively. There were 194 patients (30%) with a history of food impaction preceding diagnosis. Adults (age ≥ 18 years) comprised 56% of the cohort. Overall, the mean duration of symptoms prior to diagnosis was 7.4 ± 8.7 years.

The unadjusted association between length of symptoms and year of diagnosis as a continuous variable was significant and increased over time ($p = 0.03$) (Figure 1A). This relationship attenuated substantially within a multivariable model ($p = 0.57$) (Figure 1B), though a trend to an increased undiagnosed symptomatic period was found. The predicted length of symptoms prior to diagnosis from 2000 – 2006, 2007 – 2011, and 2011 – 2014 was 6.1, 7.2, and 7.2 years, respectively.

These findings were unchanged after stratification by child versus adult status. The length of symptoms prior to diagnosis predicted from an adjusted model for adults from 2000 – 2006, 2007 – 2011, and 2011 – 2014 was 8.3, 10.1, and 10.2 years ($p = 0.69$) (Figure 1C). A similar pattern for children was found in the corresponding years with predicted symptomatic periods of 2.8, 3.5, 3.7 years, respectively ($p = 0.32$) (Figure 1D).

Discussion

We hypothesized that the length of EoE-associated symptoms prior to diagnosis should decrease over time. Instead, we found that symptom length preceding diagnosis did not

statistically correlate with year of diagnosis and has not decreased. These findings held in both children and adults. The reason for this paradoxical finding is unknown and warrants additional study.^{1,2} It remains unclear if patients do not recognize their symptoms as a disease process, lack of referral to or unavailability of specialists, or under recognition by providers.

Limitations include the analysis of data from a single and tertiary care center, which raises concern for referral bias and poor generalizability. For example, referral patients may have more severe and/or long-standing symptoms. However, the demographic features of our cohort are typical of a non-referral population. As EoE and PPI-REE are similar in many aspects, the exclusion of PPI-responsive patients does not likely bias our results.^{3–8} It did diminish sample size and produced a less precise estimate. Also, differentiating EoE and PPI-responsive patients should prolong diagnosis by 6–8 weeks at most.¹ Strengths include the study size, inclusion of confounding covariates, and homogenous sample.

In conclusion, the length of symptoms before EoE diagnosis has not decreased over time but may be increasing. Increased efforts should be made to raise awareness of this disease. Future studies should assess these results in PPI-responsive patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

EoE	eosinophilic esophagitis
UNC	University of North Carolina

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Figure 1.

(A) Symptomatic period versus year of diagnosis for all patients; (B) Symptomatic period versus year of diagnosis for all patients predicted from multivariable model; (C) Symptomatic period versus year of diagnosis for adults predicted from multivariable model; (D) Symptomatic period versus year of diagnosis for children predicted from multivariable model