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The Prevalence and Diagnostic Utility of Endoscopic Features of Eosinophilic Esophagitis: A Meta-Analysis

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Abstract

Background & Aims—Endoscopic findings such as esophageal rings, strictures, narrow-caliber esophagus, linear furrows, white plaques, and pallor or decreased vasculature might indicate the presence of eosinophilic esophagitis (EoE). We aimed to determine the prevalence and diagnostic utility of endoscopic features of EoE.

Methods—We conducted a systematic review and meta-analysis. PubMed, EMBASE, and GI meeting abstracts were searched to identify studies that included ≥ 10 patients with EoE and reported endoscopic findings. Pooled prevalence, sensitivity, specificity, and predictive values were calculated using random- and mixed-effects models.

Results—The search yielded 100 articles and abstracts on 4678 patients with EoE and 2742 without (controls). In subjects with EoE, the overall pooled prevalence of esophageal rings was 44%, strictures 21%, narrow-caliber esophagus 9%, linear furrows 48%, white plaques 27%, and pallor/decreased vasculature 41%. Substantial heterogeneity existed among studies. Results from endoscopy examinations were normal in 17% of patients, but this number decreased to 7% when the analysis was limited to prospective studies (P<.05). Overall levels of sensitivity were modest, ranging from 15% to 48%, whereas levels of specificity were greater, ranging from 90% to 95%. Positive predictive values ranged from 51% to 73% and negative predictive values ranged from 74% to 84%.

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Author contributions:

Kim: Acquisition of data; analysis and interpretation of data; drafting/revision of the manuscript; final approval

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Conclusions—There is heterogeneity among studies in the reported prevalence of endoscopic findings in patients with EoE, but in prospective studies, at least 1 abnormality was detected by endoscopy in 93% of patients. The operating characteristics of endoscopic findings alone are inadequate for diagnosis of EoE. Esophageal biopsies should be obtained from all patients with clinical features of EoE, regardless of the endoscopic appearance of the esophagus.

Keywords

esophagus; inflammation; immune response; detection

Introduction

Eosinophilic esophagitis (EoE) is a clinicopathological disease first described in 1978 that is characterized by esophageal dysfunction and marked esophageal eosinophilic infiltration.[1, 2] Presenting symptoms differ among patient populations. Adults typically present with symptoms of dysphagia, food impactions, and heartburn.[3, 4] Although children can also present with swallowing difficulties, they most commonly have non-specific symptoms such as abdominal pain, vomiting, and failure to thrive.[5–7] EoE is a relatively new disease, so our understanding is limited; because patients often present with nonspecific symptoms, it can be a challenge to diagnose.[8]

Diagnostic guidelines for EoE were created by participants of the First International Gastrointestinal Eosinophil Research Symposium (FIGERS) in 2007, and updates to these guidelines were published in the spring of 2011.[2, 9] These diagnostic guidelines include features of the clinical presentation and histologic findings characteristic of the disease, but there are currently no recommendations regarding the role of endoscopic findings in the diagnosis of EoE.[2, 9]

Endoscopic findings of EoE include esophageal rings, strictures, narrow-caliber esophagus, linear furrows, white plaques or exudates, and pallor or decreased vasculature.[4, 10] Some studies have reported abnormal results from endoscopic examinations in as few as 33% of cases,[11–13] but other studies have reported endoscopic findings in as many as 95% of patients.[14, 15] Although some studies have reported the sensitivity, specificity, and predictive values of the presence of classic endoscopic findings of EoE,[16–19] the operating characteristics of these endoscopic findings are poorly described. We aimed to determine the prevalence, operating characteristics, and diagnostic utility of individual endoscopic features of EoE by performing a systematic review and meta-analysis of the literature.

Methods

Search Strategy and Data Collection

Two authors (HPK, RBV) independently searched the MEDLINE-indexed literature using the PubMed search engine from the National Center for Biotechnology Information (www.pubmed.gov). All studies with a print or electronic publication date from January 1, 1950 through June 30, 2011 were eligible for inclusion. To identify all relevant articles, the following search terms were used: *eosinophilic esophagitis, allergic esophagitis, corrugated esophagus, ringed esophagus, eosinophil AND gastrointestinal, eosin* AND esoph**.* The search was repeated in the EMBASE search engine to ensure that all eligible papers were reviewed, and the bibliographies of identified articles were hand searched. We also searched the published proceedings from the annual national meetings of the American Gastroenterological Association (AGA) and the American College of Gastroenterology (ACG) from 2000 to 2011.

After the search was complete, both authors reviewed each abstract to determine eligibility for inclusion. If there was any discrepancy, the full article was reviewed. Exclusion criteria comprised nonhuman studies, basic science/nonclinical studies, letters to the editor, editorials, review and summary articles, case reports, non-English studies without available translations, studies with <10 patients diagnosed with EoE, and studies that did not report upper endoscopy (EGD) findings. If studies reported a composite endoscopic score, primary authors were contacted to request original data regarding specific findings. We included case series, cross-sectional and cohort studies, case-control studies, and clinical trials. All eligible studies were included in the prevalence analysis, while the analysis of operating characteristics was restricted to studies that had a non-EoE control group.

Pertinent data were extracted from each study and organized into evidence tables independently by 2 authors. Data collected included year of publication, study design, study population (adults versus children defined as <18 years of age), number of patients in the study diagnosed with EoE, numbers of control participants (without EoE) if applicable, patients' sex and age, and all reported endoscopic findings. Endoscopic findings included: esophageal rings (which could be termed rings, felinization, trachealization, or corrugation), strictures (defined as a focal narrowing of the esophagus), narrow-caliber esophagus (defined as a diffusely narrowed esophagus without clear focal stricture), linear furrows (longitudinal grooves or crevices parallel to the length of the esophagus which could be termed linear furrows, linear fissures, or tram tracks), white plaques or exudates, pallor or decreased vasculature (defined as abnormal color, granularity, or congestion of the esophageal mucosa with loss of the normal vascular pattern), and erosive esophagitis (defined as erosions and erythema in the area of the distal esophagus and gastroesophageal junction). The number of normal endoscopies per study was also recorded. All extracted data was collected and reviewed by both authors, with discrepancies reviewed and reconciled by all of the authors.

Statistical analysis

All study findings were compiled in tabular form, and the prevalence, sensitivity, specificity, and positive and negative predictive values were calculated for each finding by study. Overall unweighted prevalence and operating characteristics were also calculated using the raw data.

Statistical analysis was performed using Stata software (version 12.0; StataCorp LP, College Station, TX). Meta-analysis was performed to determine pooled prevalence rates and 95% confidence intervals using a random-effects model and with I^2 as the measure of heterogeneity. The I^2statistic estimates the percentage of total variation across studies that is secondary to study heterogeneity. An I^2 statistic of 0% indicates no observed heterogeneity, and that all variation can be attributed to chance, whereas larger values indicate increasing heterogeneity. I^2 of 25%, 50% and 75% are considered to represent low, moderate, and high levels of heterogeneity, respectively.[20] The pooled operating characteristics (sensitivity, specificity, predictive values, and corresponding 95% confidence intervals) were determined using a mixed-effects model. To assess for sources of heterogeneity, stratified analyses were performed by age (adults vs children), study design (retrospective vs prospective), publication date (before vs after publication of guidelines), and study size (N_{EoE}<30, N_{EoE}≥30). Stratification for publication was set at 2008, due to publication of the initial diagnostic guidelines for EoE in late 2007.

Results

Search Results

Of the 1338 publications initially identified, 80 original articles and 20 abstracts were included in the prevalence analysis, including more than 4600 patients with EoE (Figure 1). A total of 995 articles were excluded: 34 letters, 11 editorials, 29 papers that were not in the English language, 151 nonclinical or nonhuman studies, 168 review or summary articles, 65 case reports, 350 studies with less than 10 patients with EoE or no reported endoscopic findings, and 430 off-topic publications. A total of 20 original articles and 4 abstracts included patients with EoE and control groups (without EoE); these were included in the operating characteristics analysis. After all data was extracted from the studies, a 10% sample of extracted data was examined and agreement between authors was excellent (kappa=0.98).

Prevalence

There was a broad overall range of findings reported among the 100 publications included in this analysis (Appendix 1). After meta-analysis, the overall pooled prevalence of esophageal rings was 44%, strictures 21%, narrow-caliber esophagus 9%, linear furrows 48%, white plaques or exudates 27%, pallor or decreased vasculature 41%, and erosive esophagitis 17% (Table 1). The endoscopic examination was normal in 17% of cases. After stratification by study design, prospective studies reported a greater prevalence of at least one abnormal endoscopic finding than retrospective studies (93% vs 80%; $P<.05$). Although not statistically significant, a greater prevalence of each of the individual endoscopic findings was reported in prospective, compared with retrospective, studies for rings, linear furrows, white plaques or exudates, and pallor or decreased vasculature (Table 1).

There was also a difference in the prevalence of findings by age. Rings and strictures were more prevalent in adults (57% and 25%, respectively) than in children (11% and 8%; $P<.05$ for each). On the other hand, white plaques and pallor or decreased vasculature were more prevalent in children (36% and 58%) than in adults (19% and 18%; $P<.05$ for each). No differences according to publication date or study size were observed.

Operating Characteristics

Twenty original articles and 4 abstracts, representing more than 950 patients with EoE and 2700 controls, were included in the analysis to determine the operating characteristics of rings, strictures, linear furrows, white plaques or exudates, and pallor or decreased vasculature. Operating characteristics for each finding by study, as well as overall unweighted operating characteristics are described in Appendices 2 and 3.

For individual findings, overall pooled sensitivities were modest and ranged from 15% to 48%, whereas pooled specificities were greater and ranged from 90% to 95% (Table 2). Overall pooled positive predictive values (PPV) ranged from 51% to 73%, and pooled negative predictive values (NPV) ranged from 74% to 84%. Rings had overall sensitivity, specificity, PPV, and NPV of 48%, 91%, 64%, and 84%, respectively. The overall sensitivity, specificity, PPV, and NPV for strictures were 15%, 95%, 51%, and 76%, and for white plaques were 27%, 94%, 67%, and 74%, respectively. The operating characteristics were slightly higher for linear furrows with a sensitivity of 40%, specificity 95%, PPV 73%, and NPV 83%. For pallor/decreased vasculature, the sensitivity, specificity, PPV, and NPV were 43%, 90%, 65%, and 79%, respectively. In contrast to the low sensitivity of individual endoscopic findings, when examining the presence of at least 1 endoscopic finding, an abnormal endoscopy had a sensitivity of 87%, specificity of 47%, PPV of 42%, and NPV of 89%.

There were significant differences in the operating characteristics of these findings by patient population according to age. Rings had greater sensitivity in adults than in children (64% vs 17%; $P<.05$; Appendix 4), whereas pallor/decreased vasculature had greater sensitivity in children than in adults (57% vs. 14%; $p<0.05$). Predictive values also differed between these patient populations. Rings, strictures, white plaques/exudates, and pallor/decreased vasculature had greater PPVs in children (79%, 75%, 89%, 74%, respectively) than in adults (56%, 43%, 40%, 28%, respectively; $P<.05$ for all comparisons). In contrast, the NPVs for these findings were greater in adults (89%, 81%, 82%, 89%, respectively) than in children (64%, 54%, 63%, 74%, respectively; $P<.05$ for all comparisons).

Heterogeneity Between Studies

There was substantial heterogeneity in the overall prevalence of endoscopic findings with I^2 values ranging from 54.4% to 98.0% (Table 1). After stratification of data, heterogeneity decreased in some categories, including esophageal rings, strictures, and narrow-caliber esophagus, but remained substantial with I^2 values ranging from 31.7% to 98.9% (Table 1). Pooled prevalence of individual endoscopic findings significantly varied by patient age (as described above, rings and strictures were significantly more prevalent in adults than in children, and white plaques/exudates and pallor/decreased vasculature were significantly more prevalent in children than in adults), indicating that a proportion of the heterogeneity among studies could be attributed to the age of the study population. No significant difference in the prevalence of individual endoscopic findings was observed according to study design, publication date, or study size, and these factors did not explain additional heterogeneity.

Discussion

EoE is an emerging disease that has increased in incidence and prevalence over the past decade.[12, 21–23] Because the clinical presentation is non-specific and there are significant variations in esophageal biopsy protocols and eosinophil counting methods, EoE can be a challenge to diagnose.[24, 25] Although endoscopic features of EoE such as esophageal rings, linear furrows, and white plaques or exudates are often considered to be typical features of EoE, these are not always identified by endoscopists.[26, 27] We conducted this systematic review and meta-analysis to determine the prevalence and operating characteristics of individual endoscopic features found in patients with EoE to assess their diagnostic utility.

This study revealed that although the prevalence of any 1 individual finding may be low, 83% of individuals reported in the literature to have EoE had at least 1 endoscopic feature of this disease. When the analysis was limited to prospective studies, which are not complicated by recall bias or errors inherent to medical record review, this number increased to 93%. The increased prevalence values calculated for prospective studies indicates that with careful assessment, endoscopic abnormalities are more likely to be found in patients with EoE, and that most patients with EoE have abnormal findings from upper endoscopy examinations. However, the sensitivity values of individual endoscopic findings were modest, and although the specificity values were higher, the predictive values were inadequate for diagnostic purposes.

The predictive values of diagnostic tests vary with disease prevalence. The prevalence of EoE depends on the population studied. For example, the prevalence of EoE has been estimated to be 0.4%–1.1% in the general population.[28, 29] In patients who present for routine endoscopy for any indication, however, the prevalence of EoE increases to approximately 6.5%, and in those undergoing an EGD for dysphagia, the prevalence is 10%–15%.[16, 26, 27]

As the prevalence of EoE decreases, the PPV (defined as the probability of disease in those with a positive test result) decreases and the NPV (defined as the probability of no disease in those with a negative test result) increases. Figure 2 illustrates this point with data from the current study. If esophageal rings were used as a diagnostic tool (sensitivity 48%, specificity 91%), the positive and negative predictive values of esophageal rings in patients presenting for EGD with dysphagia (predicted probability of EoE 10%–15%) would be 37%–48% and 91%–94%, respectively. In the general population, the prevalence of EoE is much lower, and the PPV and NPV of esophageal rings would be 5% and 99%, respectively. Therefore, the presence or absence of esophageal rings would not change the pre-test probability significantly, bringing into question the utility of any individual endoscopic finding for the diagnosis of EoE or for making decisions about obtaining esophageal biopsies in the general population. However, although the sensitivity of any individual finding is low, the literature indicates that endoscopic detection of any one of the several associated abnormalities has some clinical utility.

The other major finding from this study was the substantial heterogeneity among endoscopic findings in reported in the literature for patients with EoE. This is not surprising given that the studies included in our analysis were conducted over more than 20 years, incorporated a variety of EoE case definitions, used different study designs, and investigated different populations in different settings. To address the issue of heterogeneity, we performed analyses stratifying studies by patient age (adult vs. pediatric), study type (retrospective vs. prospective), size, and year of publication (before/after first consensus guidelines). The results indicated that a proportion of the heterogeneity can be attributed to differences in the endoscopic presentation of EoE according to patient age. We observed differences in endoscopic findings between children and adults, with rings and strictures more frequently observed in adults, whereas white plaques and pallor/decreased vasculature were more frequently found in children. in endoscopic appearance of EoE with age could result from changes that occur in the esophageal mucosa as the disease progresses, with inflammatory processes occurring at earlier stages of the disease and fibrotic processes occurring later. There are limited data on disease progression to support this hypothesis,[30–34] although a similar association has been shown from analysis of cross-sectional data.[10] We also observed differences in the sensitivities and predictive values of individual endoscopic findings between children and adults. Certain endoscopic findings might therefore have more or less diagnostic utility, depending on the age of the patient. However, because of the heterogeneity and variability among studies, the role of age in the interpretation of endoscopic findings remains unclear

It is important to acknowledge several limitations of our study. Although our search strategy was broad, it is possible that some relevant studies were not identified or included. However, 2 databases were each searched independently by 2 investigators; additional sources were identified by reviewing bibliographies and including abstracts from major gastroenterology meetings. We also minimized possible misclassification of endoscopic findings during data extraction by having 2 investigators independently extract and then reconcile the data from each study; the level of agreement between the investigators was excellent. However, because there are not widely-accepted a priori definitions for the endoscopic findings of EoE, findings from each study could not be standardized beyond the judgment of the endoscopist(s) that performed each study. In addition, we were unable to comment on the role of findings in patients who could have had esophageal eosinophilia that responded to proton pump inhibitor (PPI) therapy. A broad range of studies were included in this meta-analysis, and although many of the patients had confirmed EoE, given that many of the studies were performed before consensus guidelines for the diagnosis of EoE were established, it is possible that some patients might have had PPI-responsive eosinophilia. These factors could all contribute to the substantial heterogeneity observed among studies.

In conclusion, in a systematic review and meta-analysis of endoscopic findings from patients with EoE, we found that there is a high pooled prevalence of at least 1 endoscopic finding in patients with EoE, though prevalence rates for individual findings varied and could be low. Although individual endoscopic findings had high levels of specificity, the low sensitivity and variable predictive values make them inadequate both for the diagnosis of EoE and for the decision of whether or not to obtain biopsies. There was also substantial heterogeneity in the prevalence of these findings in the medical literature; this was due, in part, to the ages of the populations studied and also probably due to variations in the definitions of EoE. A large prospective study that includes a clear atlas of endoscopic findings, to standardize nomenclature, would be required to clarify these issues.

Our findings indicate that although a high degree of suspicion for EoE must be maintained for patients that have endoscopic features of this disease, the presence or absence of endoscopic findings is insufficient to make a diagnosis. Esophageal biopsies should be obtained from all patients who present with symptoms of EoE, regardless of the endoscopic appearance of the esophagus.

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Abbreviations

ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
EGD	upper endoscopy, esophagogastroduodenoscopy
EoE	eosinophilic esophagitis
FIGERS	First International Gastrointestinal Eosinophil Research Symposium

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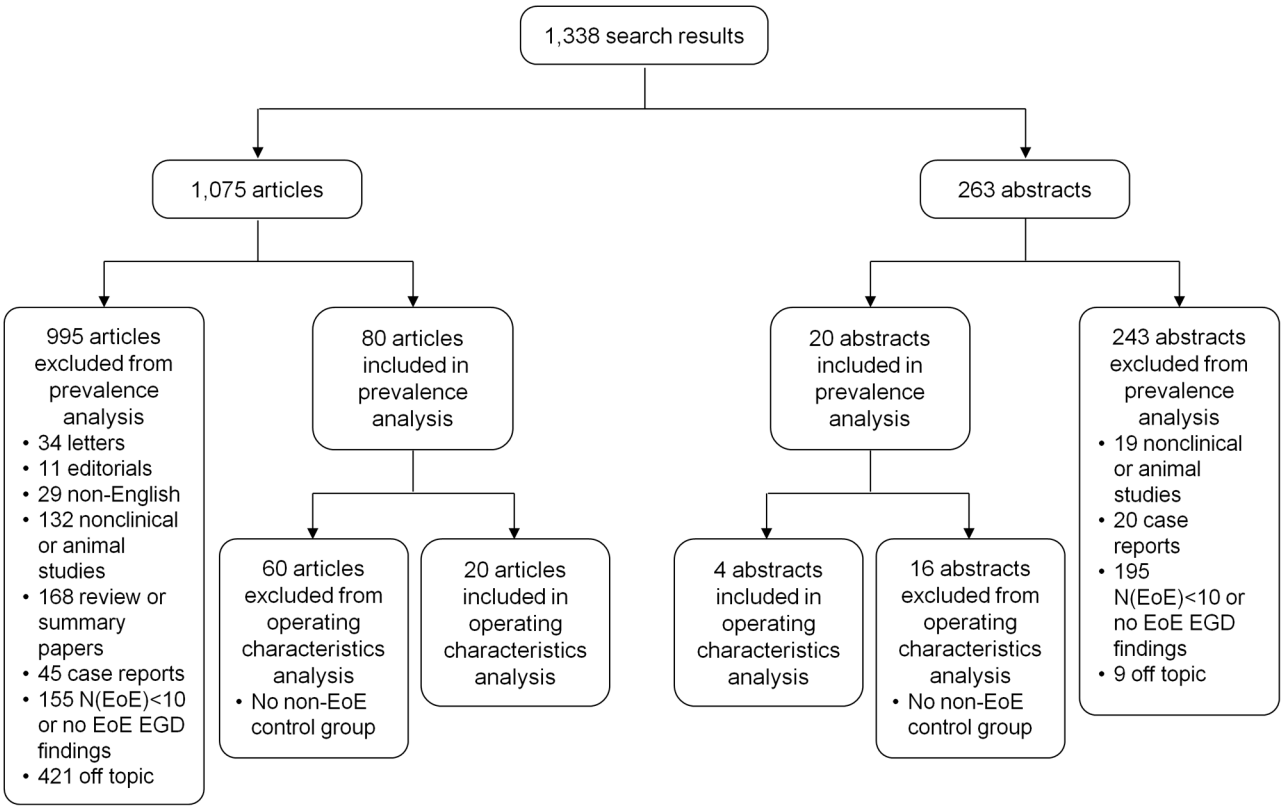


Figure 1.
Flow diagram delineating the inclusion and exclusion of studies from the prevalence and operating characteristics analyses.

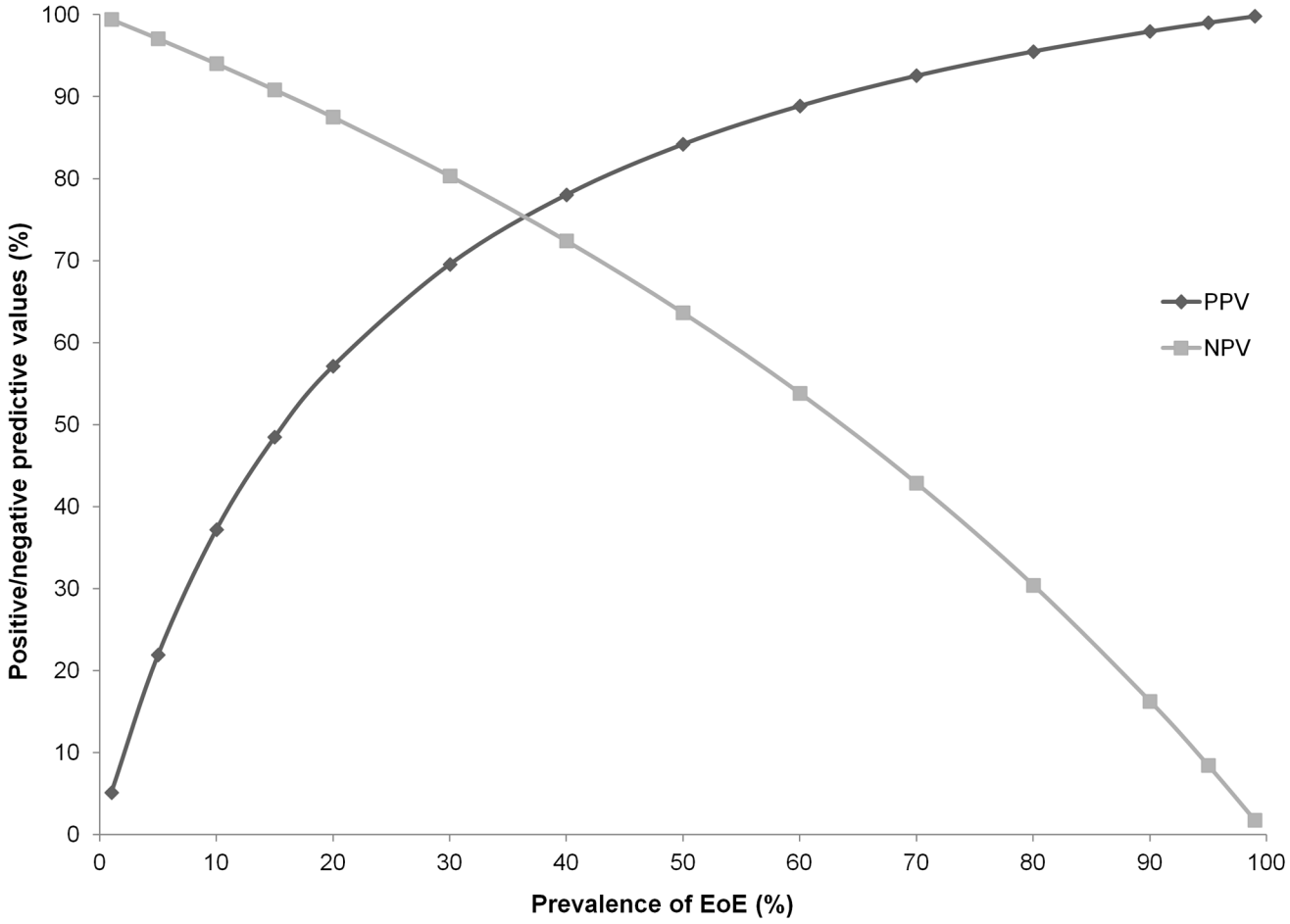
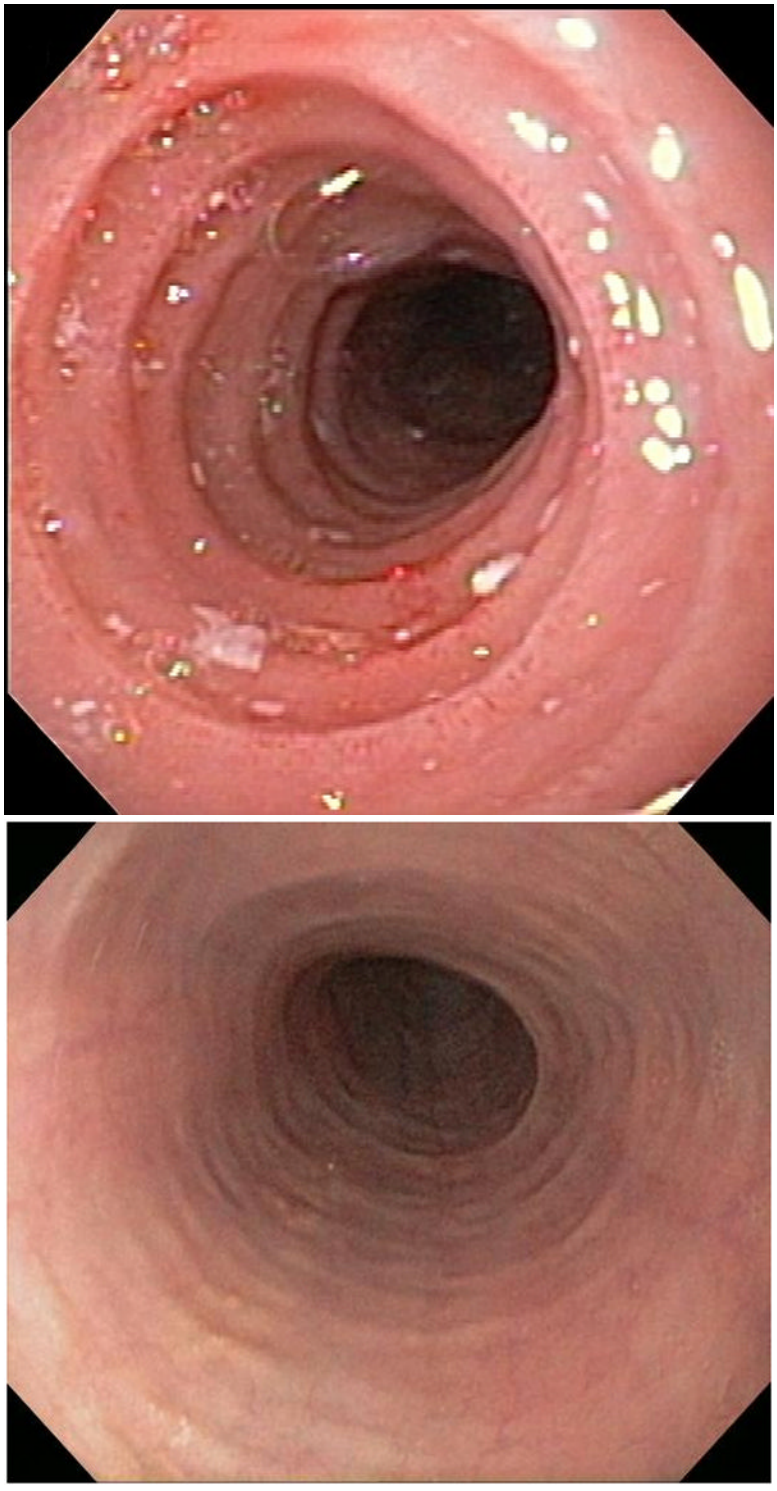
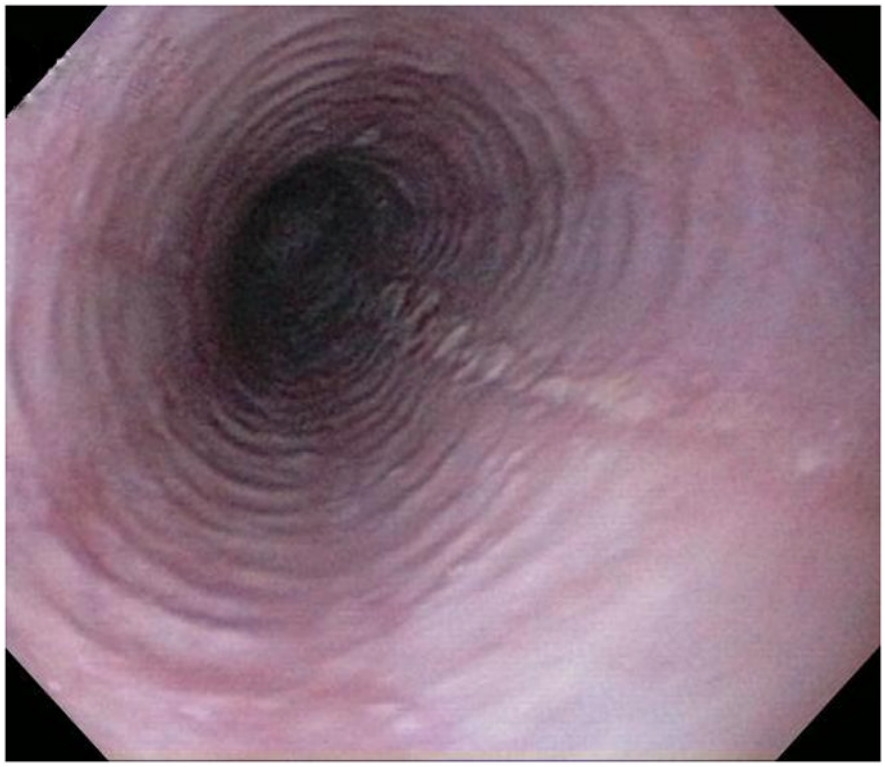
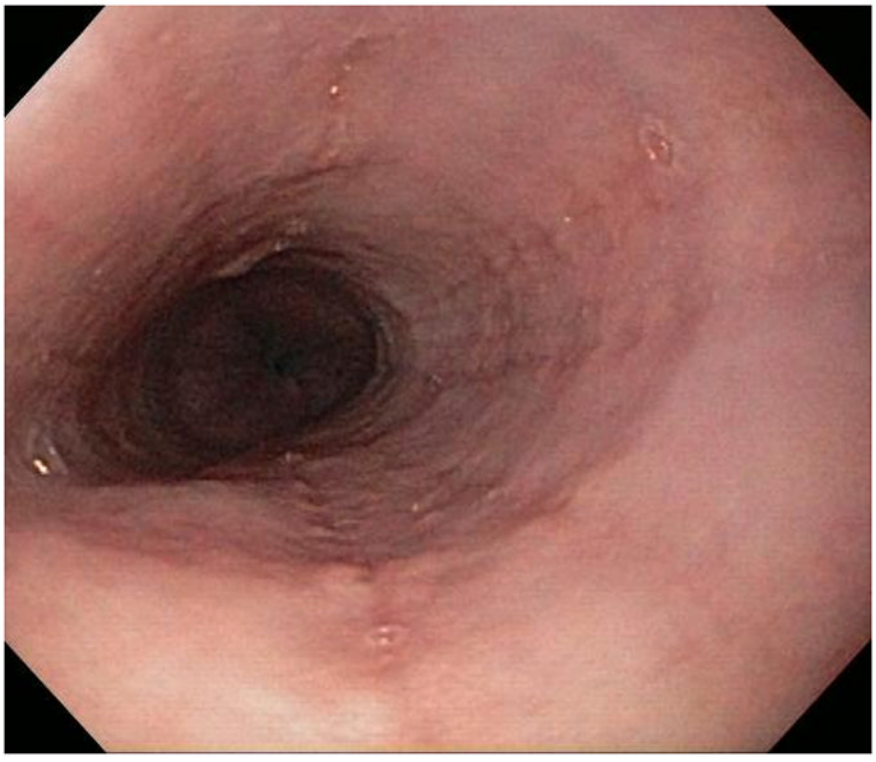


Figure 2.

The effect of EoE prevalence on the positive and negative predictive values of esophageal rings for diagnosing EoE. The sensitivity and specificity of esophageal rings are held constant at 48% and 91%, respectively, (these are the values calculated with a random-effects meta-analysis in this study), the prevalence of EoE is varied on the x-axis, and the resulting PPV or NPV are noted on the y-axis.







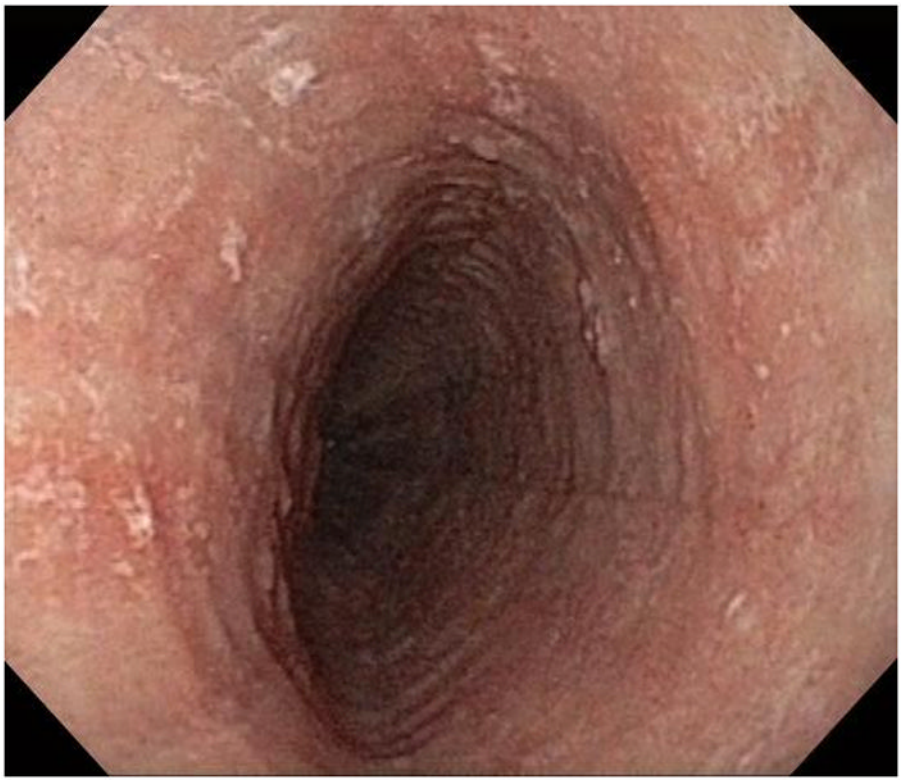


Figure 3.

Typical endoscopic findings of EoE. (**A**) Prominent and fixed esophageal rings and narrow caliber esophagus. (**B**) Subtle rings. (**C**) Rings and linear furrows, as well as mucosal pallor and decreased vasculature. (**D**) Linear furrows, mucosal pallor, and decreased vasculature. (**E**) Linear furrows and white plaques or exudates, as well as mucosal pallor and decreased vasculature.

Table 1

Prevalence of Endoscopic Findings by Study Characteristics

	Endoscopic Findings							
	Rings	**Stricture**	**Narrow Caliber Esophagus**	**Linear Furrows**	**White Plaques/Exudates**	**Pallor/Decreased Vasculature**	**Erosive Esophagitis**	**Normal**
Overall								
Prev % [95% CI] *	44 [36, 51]	21 [17, 25]	9 [7, 12]	48 [40, 56]	27 [23, 30]	41 [25, 57]	17 [13, 22]	17 [13, 22]
$N_{finding}/N_{EoE}$	1828/4313	483/2597	126/1186	1588/3967	718/4071	264/740	257/1308	838/3296
I^2 (%)	97.7	90.2	54.4	97.9	94.4	98.0	87.3	94.6
# of studies	85	46	27	77	74	21	37	66
Adults								
Prev % [95% CI] *	57 [49, 64]	25 [19, 30]	9 [6, 12]	48 [37, 59]	19 [16, 22]	18 [0, 37]	16 [11, 20]	15 [9, 21]
$N_{finding}/N_{EoE}$	1647/3149	439/2153	102/975	953/2555	331/2681	52/337	182/954	556/2159
I^2 (%)	95.9	91.9	51.4	98.3	90.2	97.6	82.1	95.6
# of studies	60	35	20	47	44	9	28	41
Children								
Prev % [95% CI] *	11 [8, 15]	8 [4, 12]	11 [5, 18]	46 [34, 58]	36 [26, 45]	58 [40, 76]	15 [7, 23]	21 [14, 29]
$N_{finding}/N_{EoE}$	134/1015	35/348	24/211	540/1263	344/1241	212/403	65/343	281/1126
I^2 (%)	64.2	58.2	62.6	96.6	94.3	95.7	85.3	92.2
# of studies	26	11	8	31	30	12	11	27
Retrospective								
Prev % [95% CI] *	39 [33, 46]	22 [17, 27]	9 [7, 12]	44 [36, 51]	22 [19, 26]	36 [19, 53]	18 [13, 24]	20 [14, 25]
$N_{finding}/N_{EoE}$	1572/3861	432/2333	114/1097	1322/3526	567/3727	183/607	213/1047	801/2918
I^2 (%)	96.8	91.6	53.9	96.7	93.3	97.6	88.9	94.8
# of studies	66	36	22	59	58	16	27	51
Prospective								
Prev % [95% CI] *	59 [43, 75]	17 [9, 25]	11 [2, 21]	61 [46, 77]	44 [29, 59]	57 [11, 102]	15 [7, 22]	7 [3, 10]
$N_{finding}/N_{EoE}$	256/452	51/264	12/89	266/441	151/344	81/133	44/261	37/378

	Endoscopic Findings							
	Rings	**Stricture**	**Narrow Caliber Esophagus**	**Linear Furrows**	**White Plaques/Exudates**	**Pallor/Decreased Vasculature**	**Erosive Esophagitis**	**Normal**
I^2 (%)	96.6	77.5	63.7	97.2	92.1	98.9	78.0	63.7
# of studies	19	10	5	18	16	5	10	15
Before 2008								
Prev % [95% CI] *	38 [27, 49]	27 [20, 34]	13 [9, 18]	50 [37, 64]	26 [18, 34]	42 [19, 65]	22 [14, 30]	16 [10, 21]
$N_{finding}/N_{EoE}$	427/1312	189/715	44/300	595/1349	284/1298	154/494	107/529	274/1367
I^2 (%)	96.7	82.0	31.7	98.1	93.2	98.5	88.7	93.2
# of studies	31	20	11	28	26	11	17	31
After 2008								
Prev % [95% CI] *	47 [37, 56]	17 [12, 22]	8 [5, 10]	46 [37, 56]	27 [23, 31]	39 [14, 64]	14 [9, 19]	18 [12, 25]
$N_{finding}/N_{EoE}$	1401/3001	294/1882	82/886	993/2618	434/2773	110/246	150/779	564/1929
I^2 (%)	97.8	91.7	55.9	97.3	93.8	97.5	85.2	95.2
# of studies	54	26	16	49	48	10	20	35
N_{EoE} <30								
Prev % [95% CI] *	43 [32, 53]	25 [15, 34]	14 [9, 19]	54 [44, 64]	36 [27, 46]	40 [17, 64]	17 [10, 24]	17 [10, 25]
$N_{finding}/N_{EoE}$	344/816	90/380	53/314	377/715	237/665	87/210	61/376	106/602
I^2 (%)	95.7	92.1	48.9	91.7	90.4	96.8	82.5	92.4
# of studies	46	21	18	40	39	12	21	36
N_{EoE} ≥30								
Prev % [95% CI] *	45 [34, 55]	19 [15, 23]	7 [4, 10]	42 [30, 53]	19 [16, 23]	41 [18, 64]	18 [12, 24]	18 [12, 24]
$N_{finding}/N_{EoE}$	1484/3497	393/2217	73/872	1211/3252	481/3406	128/355	196/932	732/2694
I^2 (%)	98.5	88.5	58.4	98.8	94.4	98.7	90.8	96.0
# of studies	40	26	9	38	35	9	17	31

* Pooled prevalence values and 95% CIs are the result of a random-effects meta-analysis.

Table 2

Overall Pooled Sensitivity, Specificity, and Predictive Values of Endoscopic Findings

	Endoscopic Findings					
	Rings	**Stricture**	**Linear Furrows**	**White Plaques/Exudates**	**Pallor/Decreased Vasculature**	**Abnormal endoscopy (≥1 finding)**
Sens % [95% CI]	48 [32, 65]	15 [10, 21]	40 [31, 51]	27 [17, 41]	43 [20, 69]	87 [80, 92]
Spec % [95% CI]	91 [81, 96]	95 [90, 97]	95 [91, 97]	94 [89, 97]	90 [82, 95]	47 [27, 67]
PPV % [95% CI]	64 [48, 81]	51 [46, 57]	73 [64, 84]	67 [57, 81]	65 [42, 91]	42 [35, 47]
NPV % [95% CI]	84 [74, 89]	76 [71, 78]	83 [79, 85]	74 [69, 77]	79 [71, 84]	89 [69, 109]
Prevalence of EoE %*	25	26	25	31	30	31
# of studies	19	11	19	14	7	14
I^2 % [95% CI]	99 [99, 100]	96 [92, 99]	98 [97, 99]	97 [95, 99]	97 [95, 99]	98 [97, 99]

*Prevalence is equivalent to the pre-test probability of having EoE, and was calculated using a mixed-effects meta-analysis.