



Optimal Diagnostic and Treatment Response Threshold of the Eosinophilic Esophagitis Endoscopic Reference Score: A Single-Center Study of 102 Patients With Eosinophilic Esophagitis

Kwangbeom Park,¹ Bokyung Ahn,² Kee Wook Jung,^{3*} Young Soo Park,^{2*} Jun Su Lee,⁴ Ga Hee Kim,⁵ Hee Kyong Na,³ Ji Yong Ahn,³ Jeong Hoon Lee,³ Do Hoon Kim,³ Kee Don Choi,³ Ho June Song,³ Gin Hyug Lee,³ and Hwoon-Yong Jung³

¹Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea; ²Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; ³Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; ⁴Department of Internal Medicine, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Chungcheongbuk-do, Korea; and ⁵Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Background/Aims

The proposed eosinophilic esophagitis (EoE) endoscopic reference score serves to diagnose and evaluate treatment responses in EoE. Nevertheless, the validated reference score thresholds for diagnosis and treatment response in Asian patients are yet to be established. This study aims to establish these thresholds for the first time among Asian patients with EoE.

Methods

Patients presenting with ≥ 15 eosinophils/high power field and esophageal dysfunction symptoms between August 2007 and November 2021 were included. Age- and sex-matched non-EoE controls were also enrolled. Baseline characteristics, endoscopic reference score features, and scores were compared between patients and controls. Among patients, endoscopic reference score features and scores, along with peak eosinophil counts, were evaluated both before and after treatment. The optimal threshold was determined based on sensitivity, specificity, and the Youden index.

Results

Overall, 102 patients were enrolled (74.5% men; mean age, 46.9 years). The mean endoscopic reference score was 2.65 and 0.52 for patients and controls, respectively ($P < 0.001$). An endoscopic reference score ≥ 2 was identified as the optimal diagnostic threshold for EoE (sensitivity, 0.79; specificity, 0.86; Youden index, 0.66). Post-treatment data regarding endoscopic findings and histology were available for 30 patients. Regarding histologic response, an endoscopic reference score of ≤ 3 demonstrated the optimal threshold (sensitivity, 0.95; specificity, 0.88; Youden index, 0.83).

Conclusions

The optimal diagnostic and treatment response thresholds were determined to be endoscopic reference scores of ≥ 2 and ≤ 3 , respectively. Further studies involving a larger patient cohort are necessary to validate these findings.

(J Neurogastroenterol Motil 2024;30:430-436)

Key Words

Endoscopy; Eosinophilic esophagitis; Esophageal motility disorders; Gastrointestinal

Received: November 6, 2023 Revised: March 22, 2024 Accepted: May 12, 2024

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Correspondence: Kee Wook Jung and Young Soo Park are equally responsible for this article.

Kee Wook Jung, MD, PhD, AGAF

Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel: +82-2-3010-3900, E-mail: jung.keewook30@gmail.com

Young Soo Park, MD, PhD

Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel: +82-2-3010-5608, E-mail: youngspark@amc.seoul.kr

Kwangbeom Park and Bokyung Ahn contributed equally to this work.

Introduction

Eosinophilic esophagitis (EoE) is a chronic allergic condition that induces inflammation in the esophagus. Its diagnosis depends on the presentation of esophageal dysfunction symptoms coupled with the detection of a substantial eosinophil count (≥ 15 per high-power field [HPF]) within the esophagus.¹⁻³ The prevalence of this condition has shown a marked rise, not only in Western countries but also in Asian nations, including Korea. This emerging trend emphasizes the urgency for further research to devise more effective diagnostic and treatment strategies.⁴⁻⁸

The EoE endoscopic reference score (EREFs) was developed to standardize the reporting of endoscopic features associated with EoE.⁹ EREFs is established based on the presence and severity of edema, rings, exudates, furrows, and strictures. EREFs has demonstrated commendable inter- and intra-observer agreement, positioning it as a prospective tool for diagnosing and assessing treatment responses in EoE patients.¹⁰ However, an optimal EREFs threshold for both diagnosis and treatment response evaluation remains to be definitively validated, particularly in Asian countries such as Korea.¹¹⁻¹⁴ In this study, we aim to identify an optimal EREFs threshold for diagnosing and histologically evaluating treatment responses among Korean patients with EoE.

Materials and Methods

Study Design and Patient Population

Patients with ≥ 15 eosinophils/HPF and symptoms of esophageal dysfunction were included retrospectively from a tertiary center in Korea between August 2007 and November 2021. Adult patients (≥ 18 years) who had undergone an endoscopic esophageal biopsy were enrolled. Exclusion criteria encompassed patients with alter-

native causes of esophageal eosinophilia, such as gastroesophageal reflux disease, parasitic infections, malignancies, collagen vascular diseases, hypersensitivity, and inflammatory bowel disease.¹⁵⁻¹⁸ Non-EoE controls constituted patients who failed to meet clinical and histologic diagnostic criteria for EoE following endoscopic esophageal biopsy. These controls were matched to EoE patients at a 1:1 ratio based on age and sex using a propensity score.

Baseline characteristics such as age, sex, and symptoms were compared between patients with EoE and non-EoE controls. A history of allergic diseases, including asthma, allergic rhinitis, food allergy, and atopic dermatitis, was assessed. Peripheral blood eosinophilia (> 500 eosinophils/ μL) and elevated IgE levels (> 100 kU/L) were defined. *Helicobacter pylori* infection confirmation relied on positive results from rapid urease, urea breath, or serology test.

Comparative analysis of EREFs features and scores between the EoE and non-EoE control groups was conducted. An optimal EREFs threshold for histologic diagnosis (≥ 15 eosinophils/HPF) was determined based on sensitivity, specificity, and the Youden index. For optimal treatment response threshold identification, EREFs features, and scores, and peak eosinophil counts were evaluated before and after treatment. The optimal treatment response threshold was determined based on sensitivity, specificity, and the Youden index for histologic response (< 15 eosinophils/HPF). The Institutional Review Board of the Asan Medical Center approved this study (Approval No. 2022-0905).

Endoscopic Examination and the Eosinophilic Esophagitis Endoscopic Reference Score Classification

Endoscopic examinations were performed utilizing a gastroduodenoscope (GIF H260 or HQ290; Olympus, Ltd, Tokyo, Japan) by 7 experienced gastroenterologists. An experienced gastroenterologist (K.W.J) retrospectively evaluated the EREFs of endoscopic images. Exudates were categorized as absent (grade 0),

mild (occupying < 10% of the esophageal surface area; grade 1), or severe (occupying > 10% of the esophageal surface area; grade 2). Rings were classified as absent (grade 0), mild (subtle circumferential ridges; grade 1), moderate (distinct rings not obstructing endoscope passage; grade 2), or severe (distinct rings obstructing endoscope passage; grade 3). Edema was determined as absent (grade 0) or present (loss of vascular markings; grade 1). Furrows were recorded as absent (grade 0) or present (vertical lines; grade 1). Strictures were categorized as absent (grade 0) or present (grade 1). The inflammatory score included exudates, edema, and furrows, with scores ranging from 0 to 4. The fibrostenotic score encompassed rings and strictures, with scores ranging from 0 to 4. The total EREFS was calculated by summing scores for all 5 features, ranging from 0 to 8.^{7,19}

Histologic Evaluation

Two pathologists, including a gastrointestinal specialist (B.A. and Y.S.P), independently re-evaluated all available hematoxylin and eosin-stained slides of esophageal biopsy specimens. They were blinded to clinicopathologic information. After scanning at a low power view, the HPF with the highest eosinophil count was selected for PEC evaluation (HPF = 0.237mm²).²⁰

Treatment and Follow-up

Treatment options encompassed proton pump inhibitors (PPIs) (standard dose, once daily), topical steroids (fluticasone from a multidose inhaler, 250–500 µg twice daily), or oral prednisolone (0.5 mg/kg/day for 6–8 weeks with dose tapering). After treatment, upper endoscopy with repeated esophageal biopsies was performed during follow-up. A histologic response was defined as a PEC of < 15 eosinophils/HPF on the follow-up biopsy.⁷

Statistical Methods

The χ^2 test or Fisher's exact test was used to compare categorical variables, whereas the Mann–Whitney *U* test was employed to assess continuous variables. Continuous variables were presented as means \pm standard deviations or numbers (%) and categorical variables as numbers (%). A *P*-value of < 0.05 denoted statistical significance. R version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) was utilized for all statistical analyses.

Results

Baseline Characteristics of Eosinophilic Esophagitis Patients and Non-eosinophilic Esophagitis Controls

A total of 102 patients with EoE and 102 non-EoE controls were enrolled. Among the EoE patients, 74.5% were men, with a mean age of 46.9 years (Table 1). The most prevalent symptom among EoE patients was dysphagia or food impaction (27.5%), followed by dyspepsia (24.5%), and heartburn (23.5%). Allergic diseases were present in 32.4% of EoE patients, including asthma, allergic rhinitis, atopic dermatitis, or food allergy. Peripheral blood eosinophilia and elevated IgE level were observed in 12.4% (12/97) and 62.2% (23/37) of EoE patients, respectively. *H. pylori* infections were detected in 35.1% (20/57) of EoE patients.

Among the 102 non-EoE controls, the most common symptom was dysphagia or food impaction (28.4%), and a higher proportion of asymptomatic patients were included compared to EoE patients (24.5% vs 0.0%, *P* < 0.001). Allergic diseases were more prevalent in EoE patients than in non-EoE controls (32.4% vs 6.9%, *P* < 0.001). The non-EoE control group included more patients with a history of alcohol consumption than the EoE control group (53.9% vs 38.2%, *P* = 0.022). Peripheral blood eosinophilia, elevated IgE levels, and *H. pylori* infection did not differ significantly between the groups.

Eosinophilic Esophagitis Endoscopic Reference Score Findings and an Optimal Diagnostic Eosinophilic Esophagitis Endoscopic Reference Score Threshold

The mean EREFS was 2.65 ± 1.41 for EoE patients and 0.52 ± 0.85 for non-EoE controls (*P* < 0.001). Furthermore, 91.2% (93/102) of EoE patients and 33.3% (34/102) of non-EoE controls had at least 1 endoscopic abnormality. Among EoE patients, 43.1% had rings, 63.7% had exudates, 74.5% had furrows, 63.7% had edema, and 5.9% had strictures. In contrast, among the non-EoE controls, 21.6% had rings, 4.0% had exudates, 8.8% had furrows, 15.7% had edema, and none had strictures (Table 2). All the EREFS features were significantly more frequent in EoE patients than in non-EoE controls. A score of ≥ 2 was the optimal diagnostic EREFS threshold, with a sensitivity of 79%, specificity of 86%, and the Youden index of 0.66 (Table 3).

Table 1. Baseline Characteristics of Eosinophilic Esophagitis Patients and Non-eosinophilic Esophagitis Controls

Variables	Patients with EoE (n = 102)	Non-EoE controls (n = 102)	P-value
Sex			
Male	76 (74.5)	76 (74.5)	1.000
Age (yr)	46.9 ± 14.7	48.2 ± 14.5	0.531
Symptoms			
Dysphagia/food impaction	28 (27.5)	29 (28.4)	< 0.001
Dyspepsia	25 (24.5)	13 (12.7)	
Heartburn	24 (23.5)	7 (6.9)	
Epigastric pain	21 (20.6)	8 (7.8)	
Nausea or vomiting	3 (2.9)	6 (5.9)	
Chest pain	1 (1.0)	3 (2.9)	
Globus	0 (0.0)	6 (5.9)	
Regurgitation	0 (0.0)	5 (4.9)	
Asymptomatic	0 (0.0)	25 (24.5)	
Allergy profile			
Asthma	15 (14.7)	5 (4.9)	< 0.001
Allergic rhinitis	12 (11.8)	2 (2.0)	
Food allergy	4 (3.9)	0 (0.0)	
Atopic dermatitis	2 (2.0)	0 (0.0)	
None	69 (67.6)	95 (93.1)	
Smoking history			
Present	39 (38.2)	45 (44.1)	0.398
None	60 (58.8)	52 (51.0)	
Unknown	3 (2.9)	5 (4.9)	
Alcohol consumption history			
Present	39 (38.2)	55 (53.9)	0.022
None	60 (58.8)	42 (41.1)	
Unknown	3 (2.9)	5 (4.9)	
Peripheral blood eosinophilia			
Present	12 (11.8)	6 (5.9)	0.318
None	85 (83.3)	81 (79.4)	
Unknown	5 (4.9)	15 (14.7)	
Elevated IgE			
Present	23 (22.5)	7 (6.9)	0.639
None	14 (13.7)	7 (6.9)	
Unknown	65 (63.7)	88 (86.3)	
<i>Helicobacter pylori</i> infection			
Present	20 (19.6)	20 (19.6)	0.807
None	37 (36.3)	31 (30.4)	
Unknown	45 (44.1)	51 (50.0)	

EoE, eosinophilic esophagitis.

Peripheral eosinophilia was defined as > 500 eosinophils/ μ L; elevated IgE level was defined as > 100 kU/L.Data are presented as n (%) or mean \pm SD.**Table 2.** Eosinophilic Esophagitis Endoscopic Reference Score Features and Scores of Eosinophilic Esophagitis Patients and Non-eosinophilic Esophagitis Controls

Endoscopic features and scores	Patients with EoE (n = 102)	Non-EoE controls (n = 102)	P-value
Exudates			
Grade 0: none	37 (36.3)	98 (96.1)	< 0.001
Grade 1: mild	55 (53.9)	2 (2.0)	
Grade 2: severe	10 (9.8)	2 (2.0)	
Score	0.74 \pm 0.63	0.06 \pm 0.31	< 0.001
Rings			
Grade 0: none	58 (56.9)	80 (78.4)	0.003
Grade 1: mild	39 (38.2)	21 (20.6)	
Grade 2: moderate	5 (4.9)	1 (1.0)	
Grade 3: severe	0 (0)	0 (0)	
Score	0.48 \pm 0.59	0.23 \pm 0.44	0.001
Edema			
Grade 0: absent	37 (36.3)	86 (84.3)	< 0.001
Grade 1: present	65 (63.7)	16 (15.7)	
Score	0.64 \pm 0.48	0.16 \pm 0.37	< 0.001
Furrows			
Grade 0: absent	26 (25.5)	93 (91.2)	< 0.001
Grade 1: present	76 (74.5)	9 (8.8)	
Score	0.75 \pm 0.44	0.09 \pm 0.29	< 0.001
Strictures			
Grade 0: absent	96 (94.1)	102 (100.0)	0.038
Grade 1: present	6 (5.9)	0 (0)	
Score	0.06 \pm 0.24	0 \pm 0	0.013
Inflammatory score	2.14 \pm 1.08	0.29 \pm 0.62	< 0.001
Fibrotic score	0.51 \pm 0.67	0.23 \pm 0.46	0.001
Total score	2.65 \pm 1.41	0.52 \pm 0.85	< 0.001

EoE, eosinophilic esophagitis.

Data are presented as n (%) or mean \pm SD.

Clinical and Endoscopic Characteristics of the Treated and Followed-up Eosinophilic Esophagitis Patients

Among the 102 patients, post-treatment data on endoscopic findings and histology were available for 30 patients. This subgroup primarily comprised men (76.7%), with dysphagia or food impaction as the predominant symptom (46.7%). Moreover, 36.6% of patients had a history of allergic diseases (Supplementary Table 1). The baseline mean EREFS was 2.83 ± 1.49 , with 60.0% exhibiting rings, 50.0% exudates, 73.3% furrows, 70.0% edema, and 13.3% strictures.

Table 3. Sensitivity, Specificity, Youden Index, Positive Predictive Value, Negative Predictive Value, and Accuracy of the Eosinophilic Esophagitis Endoscopic Reference Score Threshold for Diagnosis

EREFS threshold	Sensitivity (95% CI)	Specificity (95% CI)	Youden index (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
≥ 0	1.00 (0.96 to 1.00)	0.00 (0.00 to 0.04)	0.00 (−0.04 to 0.04)	0.50 (0.43 to 0.57)	NA	0.50 (0.43 to 0.57)
≥ 1	0.91 (0.84 to 0.96)	0.67 (0.57 to 0.76)	0.58 (0.41 to 0.72)	0.73 (0.65 to 0.81)	0.88 (0.79 to 0.95)	0.79 (0.73 to 0.84)
≥ 2	0.79 (0.70 to 0.87)	0.86 (0.78 to 0.92)	0.66 (0.48 to 0.79)	0.85 (0.77 to 0.92)	0.81 (0.72 to 0.88)	0.83 (0.77 to 0.88)
≥ 3	0.56 (0.46 to 0.66)	0.95 (0.89 to 0.98)	0.51 (0.35 to 0.64)	0.92 (0.82 to 0.97)	0.68 (0.60 to 0.76)	0.75 (0.69 to 0.81)
≥ 4	0.28 (0.20 to 0.38)	1.00 (0.96 to 1.00)	0.28 (0.16 to 0.38)	1.00 (0.88 to 1.00)	0.58 (0.51 to 0.66)	0.64 (0.57 to 0.71)
≥ 5	0.09 (0.04 to 0.16)	1.00 (0.96 to 1.00)	0.09 (0.01 to 0.16)	1.00 (0.66 to 1.00)	0.52 (0.45 to 0.59)	0.54 (0.47 to 0.61)
≥ 6	0.01 (0.00 to 0.05)	1.00 (0.96 to 1.00)	0.01 (−0.04 to 0.05)	1.00 (0.02 to 1.00)	0.50 (0.43 to 0.57)	0.50 (0.43 to 0.58)

EREFS, eosinophilic esophagitis endoscopic reference score; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; NA, not applicable.

Table 4. Sensitivity, Specificity, Youden Index, Positive Predictive Value, Negative Predictive Value, and Accuracy of the Eosinophilic Esophagitis Endoscopic Reference Score Threshold for Histologic Response (< 15 Eosinophils/High Power Field)

EREFS threshold	Sensitivity (95% CI)	Specificity (95% CI)	Youden index (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
0	0.55 (0.32 to 0.76)	0.88 (0.47 to 1.00)	0.42 (−0.20 to 0.75)	0.92 (0.64 to 1.00)	0.41 (0.18 to 0.67)	0.63 (0.44 to 0.80)
≤ 1	0.68 (0.45, 0.86)	0.88 (0.47 to 1.00)	0.56 (−0.08 to 0.86)	0.94 (0.70 to 1.00)	0.50 (0.23 to 0.77)	0.73 (0.54 to 0.88)
≤ 2	0.91 (0.71 to 0.99)	0.88 (0.47 to 1.00)	0.78 (0.18 to 0.99)	0.95 (0.76 to 1.00)	0.78 (0.40 to 0.97)	0.90 (0.73 to 0.98)
≤ 3	0.95 (0.77 to 1.00)	0.88 (0.47 to 1.00)	0.83 (0.25 to 1.00)	0.95 (0.77 to 1.00)	0.88 (0.47 to 1.00)	0.93 (0.78 to 0.99)
≤ 4	1.00 (0.85 to 1.00)	0.00 (0.00 to 0.37)	0.00 (−0.15 to 0.37)	0.73 (0.54 to 0.88)	NA	0.73 (0.54 to 0.88)

EREFS, eosinophilic esophagitis endoscopic reference score; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; NA, not applicable.

Responsiveness of the Eosinophilic Esophagitis Endoscopic Reference Score After Treatment

Thirty patients received treatment at the physician's discretion, including 19 on PPI, 4 on topical steroids, 5 on PPI plus topical steroids, and 2 on PPI plus oral steroid. Post-treatment, the mean total EREFS decreased from 2.83 ± 1.49 to 1.60 ± 1.69 ($P = 0.004$). Of the 5 EREFS features, edema, furrows, and strictures exhibited significant decrease in scores, whereas exudates and rings did not. The inflammatory score showed a significant decrease, whereas the fibrostenotic score did not (Supplementary Table 2).

The mean peak eosinophil counts dropped from 67.27 ± 106.94 to 13.67 ± 21.49 ($P = 0.009$). A histologic response was achieved in 73.3% (22/30) of patients.

Following treatment, histologic responders ($n = 22$) showed a notable decrease in mean EREFS (from 2.59 ± 1.37 to 0.91 ± 1.19), whereas histologic non-responders ($n = 8$) did not (from 3.50 ± 1.69 to 3.50 ± 1.41). The responders received PPI ($n = 13$), topical steroids ($n = 4$), PPI plus topical steroids ($n = 4$), and PPI plus oral steroids ($n = 1$) as treatment. The post-treatment inflammatory and fibrostenotic scores, along with the total EREFS for responders were 0.64 ± 0.90 , 0.27 ± 0.46 , and 0.91

± 1.19 , respectively. The corresponding scores for non-responders were 2.62 ± 1.19 , 0.88 ± 0.64 , and 3.50 ± 1.41 , respectively.

Optimal Therapeutic Response Threshold of Eosinophilic Esophagitis Endoscopic Reference Score

An EREFS of ≤ 3 was the optimal therapeutic response threshold for histologic response, with a sensitivity of 95%, a specificity of 88%, and the Youden index of 0.83. An EREFS of 0 exhibited specificity (88%) but lacked sensitivity (55%), while an EREFS of ≤ 4 demonstrated sensitivity (100%) but lacked specificity (0%) for a histologic response (Table 4).

Discussion

EREFs has proven its validity and reliability as an endoscopic scoring system in EoE, as evidenced by studies conducted in Western countries. However, the establishment of optimal diagnostic and treatment response thresholds for EREFs remains incomplete, particularly in Asian countries such as Korea. Our study aimed to establish these thresholds for Korean EoE patients.^{12,21,22} Specifically, we identified that an optimal diagnostic threshold for EREFs was ≥ 2 , while an optimal therapeutic response threshold was ≤ 3 .

To determine the optimal diagnostic EREFs threshold, we compared patients with EoE and age- and sex-matched non-EoE controls. The EoE group exhibited higher proportions of symptomatic patients and those with a history of allergic diseases. However, there were no significant differences between the groups in terms of peripheral eosinophilia, elevated IgE levels, or *H. pylori* infections. Notably, both endoscopic and histologic severity were more pronounced in EoE patients than in their non-EoE controls. Our study found that the total EREFs showed commendable diagnostic accuracy for EoE. The optimal diagnostic threshold of EREFs was ≥ 2 (sensitivity of 79%; specificity, 86%; and the Youden index, 0.66). This finding aligns with literature reports indicating that a total EREFs of ≥ 2 was optimal with a sensitivity of 88%, specificity of 92%, and area under the curve (AUC) of 0.934.¹²

After treatment, a notable reduction in the total EREFs was observed, primarily attributed to the decrease in the inflammatory score. Although the fibrostenotic score did not display a significant decrease, histologic responders exhibited a more substantial decline in EREFs compared with non-responders. Previous studies also highlighted the responsiveness of EREFs to treatments and its utility as a clinical outcome measure.^{21,23,24} Regarding histologic response, we identified EREFs ≤ 3 as the optimal therapeutic response threshold (95% sensitivity, 88% specificity, and Youden

index of 0.83). Cotton et al²² recently indicated that an EREFs ≤ 2 was the optimal clinical threshold, demonstrating a sensitivity of 80%, specificity of 83%, and an AUC of 0.793 for a histologic response (< 15 eosinophils/HPF). Some of the sub-analyses in this study suggested potential optimal thresholds of EREFs of 1 or 3, which aligns with our findings.

Our study had certain limitations. The retrospective design introduces the possibility of selection bias; however, in comparison with related studies, our research encompassed the largest cohort of Korean EoE patients. Rigorous adherence to protocols in EoE diagnosis and treatment, combined with comprehensive review of medical records and endoscopic images by trained professionals, was implemented to mitigate selection bias. Furthermore, the number of treated and followed-up patients was relatively limited owing to the rarity of EoE in Asian countries. Nonetheless, our data reflects the increasing prevalence and incidence of EoE in Korea.^{6,7} Ultimately, our study contributes valuable insights into EoE in the Korean context.

In conclusion, our study establishes that an EREFs of ≥ 2 serves as the optimal diagnostic threshold, whereas an EREFs of ≤ 3 represents the optimal treatment response threshold. Further studies involving a larger EoE patient population are necessary to validate the outcomes of our study.

Supplementary Materials

Note: To access the supplementary tables mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at <http://www.jnmjournal.org/>, and at <https://doi.org/10.5056/jnm23172>.

Financial support: None.

Conflicts of interest: None.

Author contributions: Conception and design: Kee Wook Jung; pathologic review: Bokyung Ahn, and Young Soo Park; data analysis and interpretation: Kwangbeom Park, Jun Su Lee, Ga Hee Kim, Hee Kyong Na, Ji Yong Ahn, Jeong Hoon Lee, Do Hoon Kim, Kee Don Choi, Ho June Song, Gin Hyug Lee, and Hwoon-Yong Jung; drafting the article: Kwangbeom Park, and Bokyung Ahn; and critical revision for intellectual content: Kee Wook Jung, and Young Soo Park.

References

1. Furuta GT, Katzka DA. Eosinophilic esophagitis. *N Engl J Med* 2015;373:1640-1648.
2. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 2011;128:3-20, e6.
3. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Am J Gastroenterol* 2013;108:679-692.
4. van Rhijn BD, Verheij J, Smout AJ, Bredenoord AJ. Rapidly increasing incidence of eosinophilic esophagitis in a large cohort. *Neurogastroenterol Motil* 2013;25:47-52, e5.
5. Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology* 2018;154:319-332, e3.
6. Kim HP, Vance RB, Shaheen NJ, Dellon ES. The prevalence and diagnostic utility of endoscopic features of eosinophilic esophagitis: a meta-analysis. *Clin Gastroenterol Hepatol* 2012;10:988-996, e5.
7. Kim GH, Park YS, Jung KW, et al. An increasing trend of eosinophilic esophagitis in Korea and the clinical implication of the biomarkers to determine disease activity and treatment response in eosinophilic esophagitis. *J Neurogastroenterol Motil* 2019;25:525-533.
8. Kim GH, Jung KW, Jung HY, et al. Diagnostic trends and clinical characteristics of eosinophilic esophagitis: a Korean, single-center database study. *J Neurogastroenterol Motil* 2018;24:248-254.
9. Hirano I, Moy N, Heckman MG, Thomas CS, Gonsalves N, Achem SR. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. *Gut* 2013;62:489-495.
10. Van Rhijn BD, Warners MJ, Curvers WL, et al. Evaluating the endoscopic reference score for eosinophilic esophagitis: moderate to substantial intra- and interobserver reliability. *Endoscopy* 2014;46:1049-1055.
11. Van Rhijn BD, Verheij J, Smout AJPM, Bredenoord AJ. The Endoscopic Reference Score shows modest accuracy to predict histologic remission in adult patients with eosinophilic esophagitis. *Neurogastroenterol Motil* 2016;28:1714-1722.
12. Dellon ES, Cotton CC, Gebhart JH, et al. Accuracy of the eosinophilic esophagitis endoscopic reference score in diagnosis and determining response to treatment. *Clin Gastroenterol Hepatol* 2016;14:31-39.
13. Rodríguez-Sánchez J, Barrio-Andrés J, Nantes Castillejo O, et al. The Endoscopic Reference Score shows modest accuracy to predict either clinical or histological activity in adult patients with eosinophilic oesophagitis. *Aliment Pharmacol Ther* 2017;45:300-309.
14. Reed CC, Wolf WA, Cotton CC, et al. Optimal histologic cutpoints for treatment response in patients with eosinophilic esophagitis: analysis of data from a prospective cohort study. *Clin Gastroenterol Hepatol* 2018;16:226-233, e2.
15. Gupte AR, Draganov PV. Eosinophilic esophagitis. *World J Gastroenterol* 2009;15:17-24.
16. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: proceedings of the AGREE conference. *Gastroenterology* 2018;155:1022-1033, e10.
17. Dhar A, Haboubi HN, Attwood SE, 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;71:1459-1487.
18. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J* 2017;5:335-358.
19. Schoepfer AM, Hirano I, Coslovsky M, et al. Variation in endoscopic activity assessment and endoscopy score validation in adults with eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 2019;17:1477-1488, e10.
20. Meuten DJ, Moore FM, George JW. Mitotic count and the field of view area: time to standardize. *Vet Pathol* 2016;53:7-9.
21. Wechsler JB, Bolton SM, Amsden K, Wershil BK, Hirano I, Kagalwalla AF. Eosinophilic esophagitis reference score accurately identifies disease activity and treatment effects in children. *Clin Gastroenterol Hepatol* 2018;16:1056-1063.
22. Cotton CC, Woosley JT, Moist SE, et al. Determination of a treatment response threshold for the eosinophilic esophagitis endoscopic reference score. *Endoscopy* 2022;54:635-643.
23. Dellon ES, Katzka DA, Collins MH, et al. Safety and efficacy of budesonide oral suspension maintenance therapy in patients with eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 2019;17:666-673, e8.
24. Hirano I, Dellon ES, Hamilton JD, et al. Efficacy of dupilumab in a phase 2 randomized trial of adults with active eosinophilic esophagitis. *Gastroenterology* 2020;158:111-122, e10.