Eosinophilic peak counts in eosinophilic esophagitis : a retrospective study

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Abstract

Background : **The histologic diagnosis of eosinophilic esophagitis (EoE) is based on finding >15 eosinophils/high power field (HPF) on any level within the squamous epithelium of the esophagus. However, this criterion is based on a consensus statement, and controversy remains about the exact number of eosinophils/HPF needed to diagnose EoE. We aimed to determine eosinophilic peak counts in esophageal, gastric, and duodenal biopsies from suspected EoE patients, investigate the correlation between eosinophilic peak counts at different biopsy locations, and determine inter-observer and intra-observer reliability in reporting eosinophilic peak counts.**

Methods : **We selected 103 suspected EoE patients, who underwent an endoscopic procedure between June 1, 2010 and July 15, 2017. Eosinophilic peak counts in 1 HPF were obtained by a medical student and an experienced gastrointestinal pathologist.**

Results : **Eosinophilic peak counts in suspected EoE patients are highly variable (esophagus : IQR 66-178, median 110 ; stomach : IQR 2-10, median 3 ; duodenum : IQR 16-44, median 25). No significant correlation was found between eosinophilic peak counts at different biopsy locations. The inter-observer and intra-observer correlation for reporting eosinophilic peak counts was in the near-perfect range (ρ ranged from 0.93 to 0.99, P < 0.0001).**

Conclusions : **Our data suggest that the accuracy of determining eosinophilic peak counts is not influenced by the pathologist's experience. Therefore, variability in reporting eosinophilic peak counts is unlikely to influence the diagnostic accuracy of EoE. To further improve diagnostic accuracy, investigation of other histologic features observed in EoE is needed.** (Acta gastroenterol. belg., **2019**, 82, **243-250**).

Key words : Eosinophilic esophagitis, eosinophilic peak counts, dysphagia, eosinophil

Introduction

The term eosinophilic esophagitis (EoE) was first used in 1978 to describe the esophageal lesions found in a patient with vigorous achalasia (1), but the current clinicopathologic concept of EoE has only been described in the early 1990's (2,3). Today, EoE is believed to result from an immune/antigen-mediated reaction and it is observed at any age. EoE is currently defined as "a primary clinicopathologic disorder of the esophagus, characterized by esophageal and/or upper gastrointestinal (GI) tract symptoms, with >15 eosinophils/high power field (HPF) at any level within the squamous epithelium of the esophagus. Gastric and duodenal biopsy specimens should be obtained to exclude other diseases, such as eosinophilic gastroenteritis. Absence of gastroesophageal reflux disease (GERD) has to be demonstrated by the lack of response to high-dose proton pump inhibitor (PPI) medication or a normal pH monitoring study"(4).

The most typical symptoms include dysphagia and food impaction, in addition to less frequent symptoms such as emesis, heartburn, and retrosternal chest pain (5). Endoscopic findings may include the presence of circumferential rings (also referred to as esophageal trachealization), strictures, a uniform narrowing, longitudinal furrows, mucosal edema and exsudates (6).

The current diagnostic criterion of finding >15 eosinophils/HPF at any level within the squamous epithelium of the esophagus is based on a consensus statement. However, this criterion is not uniformly accepted and controversy remains about the exact number of eosinophils/HPF needed to diagnose EoE (7). More than 10 different histopathologic definitions have been proposed in the past two decades, ranging from 5 to 30 eosinophils/HPF (8). It is well known that histologic features believed to be specific for EoE, such as intra-epithelial eosinophilia, may also be present in other esophageal diseases, mainly GERD, highlighting that high numbers of intra-epithelial eosinophils in the distal esophagus is not specific for EoE (9).

To clarify this diagnostic inconsistency, we reviewed the histopathologic features in endoscopic biopsies from Flemish patients with suspected EoE. The aim of this study was threefold : (1) to determine the peak counts of eosinophils in esophageal, gastric, and duodenal biopsies from these patients at the time of the initial diagnosis, (2) to establish if there is a correlation between eosinophilic peak counts in different biopsy locations within a single patient, and (3) to determine inter-observer reliability and intra-observer reliability in reporting these eosinophilic peak counts.

Materials and methods

Study participants and sample collection

In this retrospective study, we selected 103 patients (80 males) who consulted the department of Gastroenterology of the UZ Leuven and underwent an upper endoscopic procedure between June 1, 2010 and July 15, 2017. Patient selection was performed by querying the database of the pathology department of the UZ Leuven and extracting all cases with at least one available esophageal biopsy

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report which was coded as 'hypereosinophilic syndrome' (code 56EO, CODAP version 2017(10)).

For these patients, we reviewed the pathology reports from all biopsies taken in the University Hospital Leuven between June 1, 2010 and July 15, 2017. Samples taken prior to June 1, 2010 were excluded from this study because until that time endoscopy biopsy specimens were fixed in Carnoy's preservative, which reduces the ability to visualize eosinophils. In June 2010, the standard fixative was changed to neutral-buffered formalin 4% (11). The hematoxylin-eosin stained slides from all esophageal, gastric, and duodenal biopsies from these patients were retrieved from the lab archive for reevaluation. If available, the endoscopy reports were also extracted. These reports were manually reviewed and all relevant information was extracted and tabulated. This included the reason of the endoscopic procedure, abnormal findings during endoscopy, exact biopsy location, eosinophilic peak counts, presence of eosinophilic micro-abscesses, and other diagnoses.

Histology

Biopsy preparation and HPF selection

All biopsy specimens had been formalin fixed and paraffin embedded. 5µm sections had been cut using a microtome and according to the standard procedure in our laboratory, at least 5 serial sections were mounted on 1 glass slide. Eosinophils were visualized directly on these available hematoxylin-eosin stained slides.

To determine the maximum density of eosinophils in the tissues, their peak number in 1 HPF was counted. A small pilot study (results not shown) showed that random selection of HPFs was an unreliable method, since the number of eosinophils varied greatly within a single biopsy. Therefore, we first searched at 10x magnification the area with the highest density of eosinophils. From this area, we defined a HPF (total magnification 400x, 0.31 mm^2) using a 40x lens, and HPFs were selected to be distant from crush artefacts (12).

Eosinophil counts

Eosinophil counts were re-performed while observing the glass slide directly under the microscope (Leica DM 2000). For each HPF selected, eosinophils were counted if the nucleus or part of the nucleus was visible, together with the associated eosinophilic cytoplasmic granules. Esophageal biopsies usually contained only small fragments of lamina propria, submucosa and muscularis, therefore no separate counts were obtained in these areas. Only the number of eosinophils within the squamous epithelium was reported. In gastric and duodenal biopsies, eosinophils within the epithelium and lamina propria were counted, but not separately reported.

In all biopsy specimens, cells counts were obtained independently by a medical student (AV) and an experienced gastrointestinal pathologist (GDH), who were unaware of the patients' clinical information and ultimate diagnosis. To determine intra-observer reliability, a second read was performed by the medical student (AV) after a 3-month interval.

Data expression and statistical analysis

GraphPad statistical software (Prism, version 7.01, GraphPad Software, San Diego, CA, USA) was used to calculate relevant statistical parameters. All cell counts were reported as number of cells per HPF (cells/HPF), and the median and interquartile range (IQR) were noted when appropriate. The correlation between eosinophilic peak counts in different biopsy locations and the inter-observer and intra-observer variability was interpreted using the Spearman Rank correlation method, a non-parametric test. The influence of patient characteristics on eosinophilic peak counts was interpreted using the Mann-Whitney test, a non-parametric test. A two-tailed P value of < 0.05 was considered statistically significant.

Informed consent forms

All biopsies in the database of the pathology department of the UZ Leuven were stored with permission from the patient. Patients were aware of the fact that their residual biopsy material was stored and could be used for scientific research after the initial diagnosis was completed. Since this study was entirely performed by collecting existing data and the clinical information was anonymous, no additional informed consent was necessary.

Results

Review of initial pathology reports

In total, we evaluated the pathology reports from 103 patients (median age at the time of diagnosis : 32 y ; range 1 y to 76 y ; 80 men and 23 women), on which the initial diagnosis of EoE was based.

Biopsy location

In 54 of the 103 patients, biopsies from multiple levels in the esophagus were available (16 patients with biopsies from the distal, middle and proximal esophagus ; 35 patients with distal and proximal esophageal biopsies, and 3 patients with distal and middle esophageal biopsies). In 43 reports, the specific origin of the esophageal biopsy (distal, middle or proximal) was not noted. Gastric biopsies were taken simultaneously in 49 patients ; duodenal biopsies were taken in 30 patients.

Eosinophilic peak counts

Eosinophilic peak counts in the esophagus were noted in 87 of the 103 reports (median 54 eos/HPF, IQR 33-100) (Figure 1. A). In 32 of the 52 proximal esophageal biopsies, eosinophilic peak counts were noted (median 36 eos/HPF, IQR 20-63). In 11 of the 19 mid esophageal

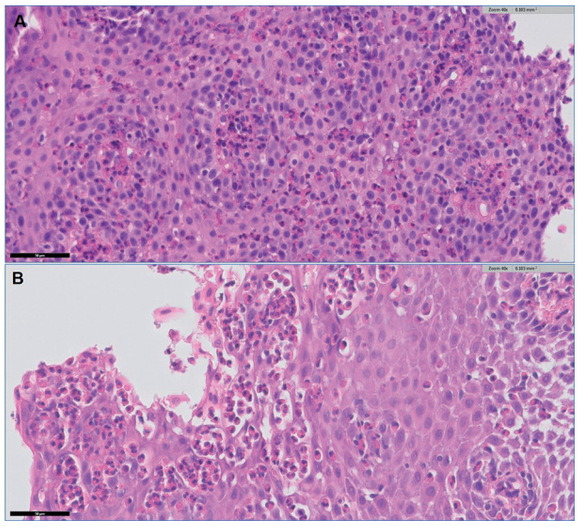

Figure 1.

biopsies, eosinophilic peak counts were noted (median 60 eos/HPF, IQR 28-73). In 36 of the 59 distal esophageal biopsies, eosinophilic peak counts were noted (median 50 eos/HPF, IQR 20-100).

Other histologic diagnoses

GERD was listed as a potential diagnosis by the pathologist in 16 patients. The presence of eosinophilic micro-abscesses was noted in 9 patients (Figure 1. B). Other potential diagnoses included Candida infection in 1 patient, allergic reaction to food or medication in 1 patient, and columnar-lined esophagus (CLE) in 1 patient. Eosinophilic peak counts were not noted for gastric or duodenal biopsies, and no increased eosinophilic infiltration was mentioned.

Number of tissue fragments

In 84 of the 103 pathology reports, the pathologist mentioned the number of esophageal tissue fragments (IQR 2-6 fragments, median of 4) together with the eosinophilic peak count in the esophagus. No significant correlation was found between the number of tissue fragments obtained during endoscopy and the eosinophilic peak counts (Spearman r : - 0.02136, 95% CI (-0.2408 to 0.2001) (Figure 2).

Review of endoscopy reports

We retrieved the endoscopy reports, which led to the initial diagnosis of EoE, from 79 (77%) of the 103 patients, and extracted all clinical information and macroscopic abnormalities mentioned in the endoscopy reports.

Indications for performing upper gastrointestinal endoscopy

In 76 (96%) of the 79 reports, the indication for performing the endoscopic procedure was mentioned.

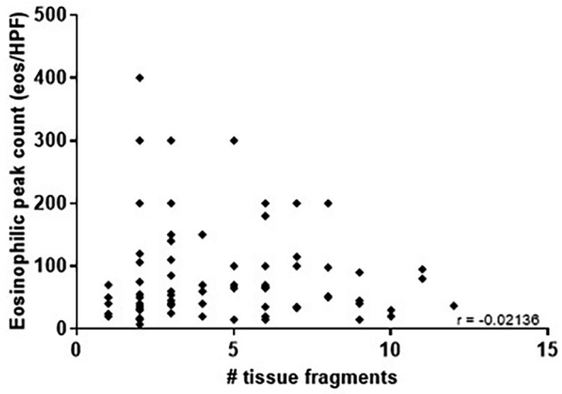

Figure 2.

The most common indications included dysphagia, noted in 38 patients (50%), "suspicion of EoE" in 14 patients (18%), and food impaction in 12 patients (16%). Other reasons included heartburn (11%), emesis (7%), follow-up endoscopy for suspected GERD (5%), and food allergy (4%).

Endoscopic findings

The most common endoscopic abnormalities seen in patients with EoE were the presence of multiple circumferential rings, seen in 31 patients (39%), linear furrows in 22 patients (28%), and a sliding hiatal hernia in 21 patients (27%) (Figure 3. A-C). Other findings included a uniform narrowing of the esophagus seen in 15 patients (19%), a Schatzki ring (15%), white exudate on the mucosal surface (18%) (Figure 3. D), edematous mucosa (13%), and an impacted food bolus (6%). In 16 patients (20%) the endoscopy report explicitly mentioned a normal appearance of the esophageal mucosa.

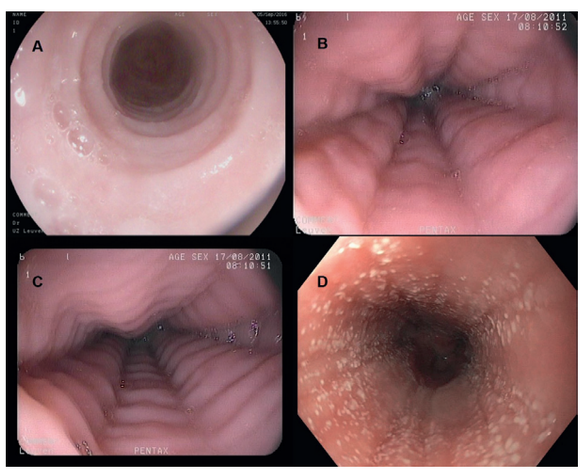

Figure 3.

Review of hematoxylin-eosin stained slides

In total, we retrieved and reviewed 462 hematoxylin-eosin stained slides from 94 patients. The slides of 9

patients could not be retrieved from the lab archive. For 37 patients, slides from multiple endoscopic procedures were available. In total, this included 254 esophageal biopsies (108 proximal esophageal biopsies, 30 middle esophageal biopsies, 116 distal esophageal biopsies), 94 gastric biopsies, and 67 duodenal biopsies obtained during 180 different endoscopic procedures. In 47 patients, multiple hematoxylin-eosin stained glass slides were available for a single biopsy location. In these cases, all glass slides were reviewed and only the highest cell count among the different glass slides was noted for a single location.

Inter-observer and intra-observer variability

To calculate inter-observer and intra-observer variability in reporting eosinophilic peak counts, all 462 hematoxylin-eosin stained slides were reviewed and the peak number of eosinophils in 1 HPF was counted. For the purpose of this part of the study, the diagnosis and patient characteristics were not relevant. Therefore, we included both initial biopsies as well as follow-up biopsies to extend the range of eosinophil counts (0 to 650 eosinophils/HPF) (13). Near-perfect inter-observer and intra-observer correlation coefficients were found in reporting eosinophilic peak counts of esophageal, gastric and duodenal biopsies (Figure 4). The Spearman's rank correlation coefficients for the inter-observer and intra-observer variability are reported in Table 1 and Table 2, respectively. Furthermore, we found a near-perfect inter-observer and intra-observer correlation coefficient for reporting eosinophilic peak counts in proximal, middle, and distal esophageal biopsies.

Eosinophilic peak counts

We reviewed all biopsies from 94 endoscopic procedures on which the initial diagnosis of EoE was based. Eosinophilic peak counts were determined by taking the highest peak count observed by either of the two observers (Table 3). For 4 endoscopic procedures, review of the esophageal biopsies led to an eosinophilic peak count lower than 15 eosinophils/HPF. We found no significant association between eosinophilic peak counts and clinical manifestations (i.e. dysphagia) (Figure 5). Additionally, no significant association was found between the density of the eosinophilic infiltrate and the presence of endoscopic findings (i.e. linear furrows, multiple circumferential rings, normal gross appearance of the esophagus).

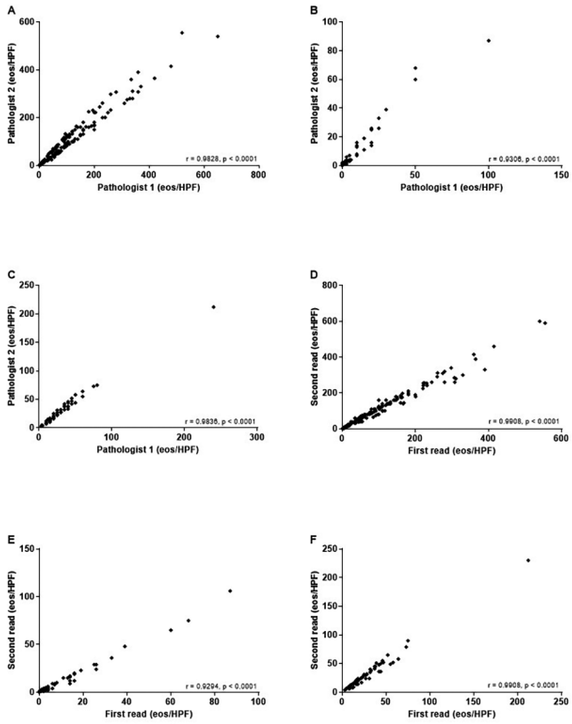

Figure 4.

Table 1. — **Inter-observer variability in reporting eosinophilic peak counts**

	Esophagus	Stomach	Duodenum
Spearman's rank correlation coefficient	0.9828	0.9306	0.9836
95% confidence interval	0.9768 – 0.9873	0.8959 – 0.9540	0.9730 – 0.9901
P value	<0.0001	<0.0001	<0.0001
Significant?	Yes	Yes	Yes
Number of biopsies	180	94	67

Table 2. — **Intra-observer variability in reporting eosinophilic peak counts**

	Esophagus	Stomach	Duodenum
Spearman's rank correlation coefficient	0.9908	0.9294	0.9736
95% confidence interval	0.9875 to 0.9932	0.8942 to 0.9532	0.9566 to 0.9840
P value	<0.0001	<0.0001	<0.0001
Significant?	Yes	Yes	Yes
Number of biopsies	180	94	67

Table 3. — **Eosinophilic peak counts in different biopsy locations**

	Proximal esophagus	Middle esophagus	Distal esophagus	Peak count esophagus	Stomach	Duodenum
Median	45	79	75	110	3	25
IQR	20-123	9-144	32-123	66-178	2-10	16-44
Max	480	330	390	650	60	240
Min	0	2	2	1	0	10
Number of biopsies	51	19	57	94	46	27

Table 4. — **Correlation between eosinophilic peak counts in different biopsy locations**

	Esophagus & Stomach	Esophagus & Duodenum	Stomach & Duodenum	Proximal esophagus & Distal esophagus	Proximal esophagus & Middle esophagus	Middle esophagus & Distal esophagus
Spearman's rank correlation	-0.08303	0.05	-0.05927	0.1461	0.1054	0.008814
95% confidence interval	-0.3722 to 0.2208	-0.3469 to 0.4317	-0.4539 to 0.3548	-0.1524 to 0.4203	-0.4251 to 0.582	-0.4587 to 0.4725
P value	0.5833	0.8044	0.7784	0.3216	0.6977	0.9714
Significant?	No	No	No	No	No	No
Number of biopsies	46	27	25	48	16	19

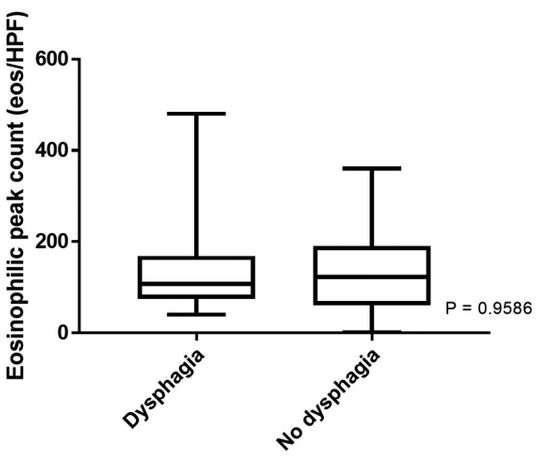

Figure 5.

Correlation between esophageal, gastric and duodenal biopsies

No significant correlation was found between eosinophilic peak counts in esophageal, gastric, and duodenal biopsies at the time of the initial diagnosis (Table 4). Additionally, no significant correlation was found between proximal, middle, and distal esophageal biopsies.

Discussion

The diagnosis of EoE is based on a combination of non-pathognomonic clinical symptoms, endoscopic signs, and histopathologic features. An eosinophilic peak count of >15 eosinophils/HPF at any level within the squamous epithelium of the esophagus is considered to be the diagnostic histopathologic criterion of EoE. However, this definition is largely based on expert opinion and different diagnostic thresholds have been proposed in the recent literature. Furthermore, current consensus guidelines imply that counting eosinophils is a reliable method to assess esophageal eosinophilia (13). To clarify this diagnostic inconsistency and to investigate the reliability of reporting eosinophil counts, we conducted an observational, retrospective study that reviewed the histopathologic features observed in endoscopic biopsies from Flemish patients with suspected EoE.

This study confirms the wide range of eosinophilic peak counts observed in esophageal biopsies from suspected EoE patients. No significant correlation was found between eosinophilic peak counts at different biopsy locations within a single patient. The inter-observer and intra-observer correlation for reporting eosinophilic peak counts was in the near-perfect range (ρ ranged from 0.93 to 0.99, $P < 0.0001$).

Dysphagia and food impaction were reported in 50%, and 16% of patients, respectively. This is consistent with previous studies, which reported wide ranges of 16-100% for dysphagia, and 10-50% for food impaction (14). The prevalence of other clinical manifestations in our study was lower compared to existing data. However, we reviewed the endoscopy reports which only provided the main indication for performing the endoscopic procedure which probably led to underreporting of symptoms. For example, if the endoscopist mentioned 'suspicion of EoE' as the main indication of the endoscopy, it is unknown whether the patient had symptoms of dysphagia,

heartburn, etc. Review of the outpatient clinic files may have provided a more complete overview of clinical symptoms, but was not performed in this study due to restrictions concerning the ethical approval.

No significant association was found between the density of the eosinophilic infiltrate and the presence of dysphagia, which leads us to hypothesize that the epithelial eosinophilic infiltrate is not directly linked to the presence of clinical symptoms. Previously published data on this topic are conflicting, which can be at least partly explained by differences in the assessment of clinical symptoms, and inclusion of different study populations. The EoE Activity Index Study, which used a standardized instrument to measure patient-reported outcomes, found more severe symptoms in adult patients with more than 320 eosinophils/mm² (approximately 100 eosinophils/HPF) (15). In pediatric EoE patients, a dissociation between symptoms and histological severity has been observed, with symptoms persisting in 85% of patients with histologic resolution (16). This indicates that scheduling a follow-up biopsy based on persisting clinical symptoms might not relate to finding histologic abnormalities. Based on our findings, which included both pediatric and adult patients (range 1 y to 76 y), we suggest that resolution of clinical symptoms not necessarily implies concurrent histologic normalization. Therefore, a follow-up biopsy is indicated regardless of clinical symptoms. Nonetheless, it remains unclear whether follow-up biopsies affect long-term clinical outcome at all, e.g. for the development of strictures. At this moment there is no concern of secondary malignancy since no squamous dysplasia has been observed in long-standing EoE (17).

The presence of multiple circumferential rings, and the presence of linear furrows were the most common endoscopic abnormalities found in our patients. Due to inconsistent reporting and differences in the interpretation of endoscopic findings by various gastroenterologists, our study might underestimate the true prevalence of endoscopic findings. Based on the observation that there was no significant association between endoscopic findings (i.e. multiple circumferential rings, or linear furrows) and the density of the eosinophilic infiltrate, one might hypothesize that endoscopic abnormalities are no direct consequence of the eosinophilic infiltrate. This is in line with a recent study which found no correlation between endoscopic findings and histological disease activity in adult EoE patients, except for a correlation between exudates and eosinophilic peak counts (18). A recent prospective study reported that biopsies taken in areas of exudates and furrows resulted in increased eosinophilic counts (19). Since our study included biopsies taken by various gastroenterologists, including fellows in training, following different biopsy protocols, our results need to be interpreted with caution. Interestingly, 20% of our patients presented with a normal gross appearance of the esophageal mucosa. Again, no association with the density of the eosinophilic infiltrate was observed, supporting the hypothesis that there is no direct link between the eosinophilic infiltrate and endoscopic abnormalities. This further highlights the importance of routine biopsy taking, regardless of the macroscopic appearance of the esophagus, but also the systematic reporting of the endoscopic appearance of the esophagus using a validated scoring method.

Recently, the use of the endoscopic reference score (EREFS) was proposed, which provides a uniform scoring system for endoscopic findings in suspected EoE patients (20). It enables the endoscopist to consistently report the presence of exudates, rings, edema, furrows, and strictures in the esophagus. Development of a similar scoring method for assessing histopathologic features in EoE might lead to a more consistent method for reporting histologic abnormalities, which promotes the recognition of these abnormalities, and might ultimately facilitate the histologic diagnosis of EoE. Review of our pathology reports led to the observation that eosinophilic peak counts were reported in a majority of cases. However, other histologic features which are associated with EoE were inconsistently reported and could therefore not be extracted from the original pathology reports. In 2016, a histologic scoring system for EoE was presented, which promotes systematic interpretation of different histologic features observed in EoE patients (21). This includes the presence of eosinophilic inflammation and abcesses, basal zone hyperplasia, dilated intercellular spaces, lamina propria fibrosis, eosinophil surface layering, surface epithelial alteration, and the presence of dyskeratotic epithelial cells. In the future, the systematic use of this histologic scoring system might improve the accuracy of the histologic diagnosis of EoE.

We found no correlation between the number of esophageal tissue fragments obtained during the endoscopic procedure, and the eosinophilic peak counts. This observation was unexpected, since the eosinophilic infiltrate is patchy, and we expected that obtaining more tissue fragments would result in a higher eosinophilic peak count. This might be accounted for by the variable size of the tissue fragments, and we further suspect that when distinct endoscopic abnormalities were present, the endoscopist might collect less esophageal tissue fragments.

In approximately 50% of patients, the exact esophageal biopsy location was not mentioned in the endoscopy report or only a distal biopsy was available. Since a previous study indicated that high numbers of intra-epithelial eosinophils are not specific for EoE, it might be impossible for the pathologist to rule out GERD-induced eosinophilia in distal biopsies (9). Clinicians should therefore be motivated to specify the exact biopsy location. Furthermore, since histopathologic features can only be accurately assessed in a suggestive clinical context, clinicians should reveal all relevant clinical information to the pathologist. Current diagnostic guidelines recommend biopsy taking from different locations in the esophagus. Gastric and duodenal tissue

samples should also be obtained to exclude other diseases, such as eosinophilic gastroenteritis or chronic inflammatory bowel diseases.

Based on our findings, we speculate that systematic reporting of eosinophilic peak counts in gastric and duodenal biopsies might be of potential benefit. For example, we observed a duodenal eosinophilic peak count of 240 in a particular patient, which was not mentioned in the original pathology report, but might have had significant influence on the diagnostic process, since eosinophilic gastroenteritis should have been excluded. Moreover, the prognosis of eosinophilic gastroenteritis depends on a timely and proper treatment (i.e. oral steroids) (22). However, interpretation of eosinophilic peak counts is hampered by the lack of normal reference values for eosinophils in the stomach and duodenum. A recent study suggested a cut-off count of 20 eos/HPF to separate patients with normal from those with elevated duodenal eosinophilia (23). Our study revealed a median peak count of 25 eos/HPF in the duodenum, which might indicate that the majority of patients with eosinophilic esophagitis have associated elevated duodenal eosinophilic infiltrations. We further demonstrated that there was no correlation between eosinophilic peak counts in the esophagus, stomach, and duodenum within a single patient. The added value of obtaining gastric and duodenal biopsies during follow-up endoscopies might therefore be limited to exclusion of other abnormalities, though previous studies reported conflicting evidence (24).

We found a near-perfect inter-observer and intra-observer correlation for reporting eosinophilic peak counts, which is in line with previous studies on this topic (13,25). This is of importance because the histologic diagnosis of EoE highly depends on accurate determination of eosinophilic peak counts. Based on our findings, we can state that variation in reporting eosinophilic peak counts does not likely contribute to the diagnostic inconsistency observed in EoE. To our knowledge, this is the first study that demonstrated that eosinophil counts can be accurately determined by medical students. However, a previous study reported highly accurate determination of eosinophil counts by pathology trainees (25). Based on these findings, we speculate that experience in pathology reporting has no significant influence on the accuracy of determining eosinophil counts. This certainly implies that all board-certified pathologists can accurately assess eosinophil counts. With the rapidly increasing incidence and prevalence of EoE it is to be expected that pathologists will be increasingly faced with biopsy specimens from suspected EoE patients (26).

Our study has several limitations which must be considered when interpreting these results. First, patient selection was performed retrospectively, based on the pathology report and if available, clinical and endoscopic findings. Therefore, the diagnosis of EoE may have been questionable in some cases, since other causes of tissue eosinophilia, such as GERD, could not strictly be ruled out in some patients solely based on the existing pathology report. The presence of clinical symptoms could only be based on the major symptom indicated by the endoscopist. Second, cell counts were only performed by two observers and the medical student was not systematically trained to report eosinophil counts prior to this study. Despite the large sample size, extrapolation of these results to draw general conclusions about inter-observer and intra-observer correlation for reporting eosinophil counts should be done with caution. Finally, this study only re-assessed eosinophilic peak counts, inclusion of other histologic features could have revealed additional data.

In conclusion, we report a near-perfect inter-observer and intra-observer correlation for reporting eosinophil counts in suspected EoE patients, which indicates that reporting of eosinophil counts does not contribute to the diagnostic variability of EoE. In order to increase the diagnostic uniformity among researchers and clinicians, we propose the further implementation of the EREFS score in routine practice and the implementation of a validated scoring system which allows a more uniform recognition, interpretation and reporting of histologic features observed in EoE.

Conflict of Interest

None

Financial Disclosure

None

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