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Yield of Esophageal Biopsy Patterns for the Diagnosis of Eosinophilic Esophagitis

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This article reviews Muftah M, Harnett DA M, Hiramoto B, et al. Yield of Esophageal Biopsy Patterns for the Diagnosis of Eosinophilic Esophagitis. Gastrointest Endosc. 2025 Aug;102(2):194-201.

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STRUCTURED ABSTRACT

Question: Does the currently recommended biopsy protocol for the diagnosis of eosinophilic esophagitis (EoE), 6 samples from the distal and either proximal or middle esophagus, adequately capture EoE diagnoses, or is the diagnostic yield improved by altering biopsy site selection?

Design: Retrospective, cross-sectional study of consecutive treatment naive adult patients with newly diagnosed EoE with ≥2 esophageal segments biopsied. Distribution of eosinophilia (≥15 eosinophils [eos]/high-power field [hpf]) in the proximal, middle, and distal esophagus was assessed.

Setting: Three hospitals (2 community and 1 tertiary care center) from 2017-2021.

Patients: Adults presenting with symptoms of esophageal dysfunction and

histopathology showing ≥ 15 eos/hpf on at least 1 esophageal biopsy. All included patients had biopsy samples obtained from ≥ 2 esophageal segments (distal, middle, and/or proximal). Among 727 newly diagnosed patients, mean age was 43.4 ± 14.9 years; 55.9% were male and 89.3% were White. On the index EGD, patient biopsy samples were obtained from 1, 2, and 3 esophageal segments in 216 (29.7%), 451 (62%), and 60 (8.3%) patients, respectively. Thus, 511 patients met inclusion criteria.

Interventions/Exposure: Distribution of esophageal eosinophilia assessed by biopsy site (distal, middle, proximal). Proportion of patients with non-distal disease (<15 eos/hpf in distal biopsies) and segmental eosinophilia patterns were determined.

Outcome: The primary outcome was the distribution of esophageal eosinophilia at the time of diagnostic EGD. Biopsy site was determined by review of endoscopy and pathology reports. Biopsies samples obtained from different sites were placed in separate bottles and labeled as either proximal (proximal to 23 cm), middle (24 to 31 cm), or distal (distal to 32 cm) esophagus. For those with biopsies from 2 sites, proportion of patients with ≥15 eos/hpf from both sites versus 1 site was assessed. For those with 3 sites biopsied, proportion with ≥15 eos/hpf from all 3 biopsy sites versus 2 sites or 1 was assessed. Other outcomes included concordance of esophageal eosinophilia in the proximal and mid esophagus as well as the proportion with and factors associated with non-distal disease.

Data Analysis: Demographic, clinical, endoscopic, and histologic variables of subjects were summarized by using descriptive statistics. Distribution (proximal, middle, and/or distal) of eosinophilia (≥15 eos/hpf) was assessed. Predictors for non-distal disease (<15 eos/hpf on distal biopsy samples) were evaluated by using multivariable logistic regression.

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Results: Among 511 patients with biopsy samples obtained from ≥2 segments, endoscopic features of EoE were seen in 330 (64.6%) and all patients had distal biopsy samples. In this group, 56% had ≥ 1 site with < 15 eos/hpf, and 10% had non-distal disease (i.e., no distal eosinophilia). Among the 254 patients with only 1 site displaying eosinophilia (≥ 15 eos/hpf), 210 (82.7%) had eosinophilia only in the distal segment,

whereas 44 (17.3%) had eosinophilia only in the proximal or middle segment (**Figure 1**).

In those with biopsies from all 3 segments (n=60), 31.7% had eosinophilia in only 1 segment, including 10% with isolated mid esophageal disease and no isolated proximal eosinophilia (**Figure 2**). Discordance between middle and proximal biopsy results occurred in 30% of patients, with 94.4% showing eosinophilia in the middle but not the proximal esophagus. On multivariable analysis, increasing age (odds ratio, 1.02; 95% CI, 1.002-1.04; $P = 0.03$) and male sex (odds ratio, 1.89; 95% CI, 1.002-3.55; $P = 0.049$) were independent predictors of non-distal disease.

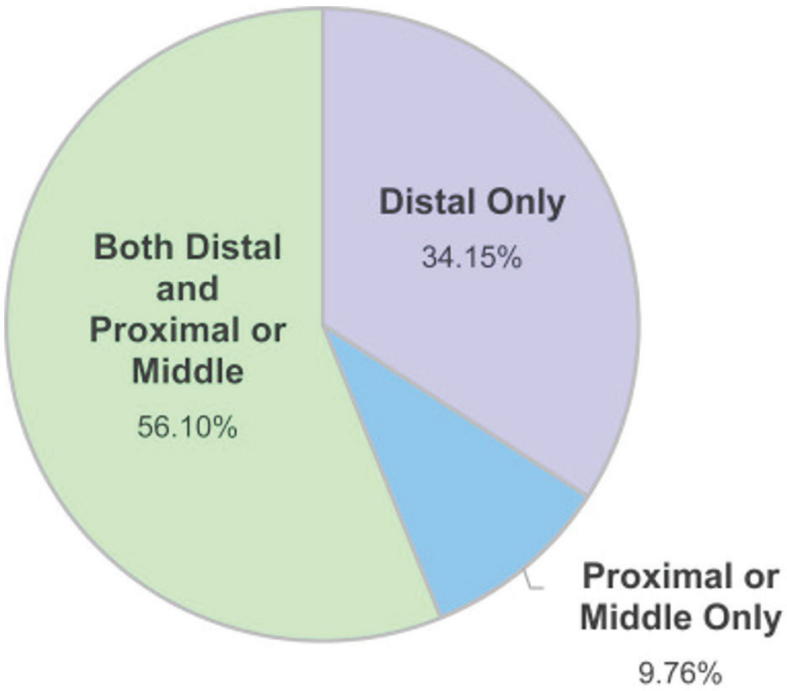

Figure 1. Distribution of eosinophilia in patients with biopsies of 2 esophageal segments.

COMMENTARY

Why Is This Important?

Current consensus guidelines[1] for the diagnosis of EoE recommend obtaining at least 2-4 biopsies from 2 locations in the esophagus: the distal esophagus and either the mid or proximal esophagus. These recommendations are based on limited data[2-4] supporting some key assumptions that (1) nearly all patients with EoE have distal eosinophilia and thus biopsies from this area will have a 100% diagnostic yield; (2) middle and proximal esophageal biopsy specimens are interchangeable; and (3) very few patients have disease isolated to a single esophageal segment. This study is the largest to date to assess the pattern and location of esophageal eosinophilia

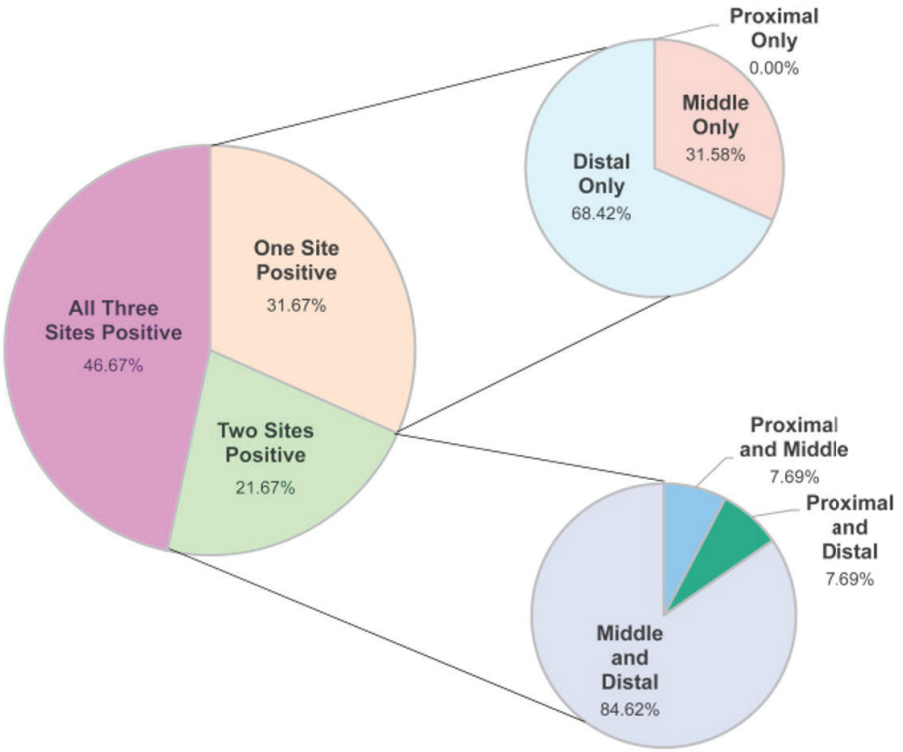

Figure 2. Distribution of eosinophilia in patients with biopsy samples from all 3 esophageal segments.

at the time of initial EoE diagnosis with some findings that potentially challenge current biopsy acquisition recommendations for EoE diagnosis.

Key Study Findings

Aligned with guideline recommendations, 90% of the cohort had distal eosinophilia. However, the study showed that 10% of the cohort had non-distal disease and 30% had discordant findings between eosinophilia in the proximal and middle segment biopsies, with > 90% of them having middle but not proximal eosinophilia. Additionally, 31.7% met diagnostic criteria for EoE with ≥ 15 eos/hpf in only 1 esophageal location. Study findings support current recommendations to obtain multiple biopsies from different locations in the esophagus to maximize the diagnostic yield of EoE.

The results do question the current recommendations that treat mid and proximal esophageal biopsies interchangeably, as in this study the frequency and pattern of discordance in eosinophilia supports greater yield from biopsies obtained from mid esophagus rather than the proximal esophagus. Importantly, although 10% of patients in the subgroup with all 3 sites biopsied had isolated eosinophilia in the middle esophagus, none had proximal-only eosinophilia. Thus, this 10% of patients with EoE could be missed if biopsies were just obtained from the distal and proximal esophagus, which translates to approximately 3,600 missed cases of EoE annually in the United States.[5]

While, independent predictors for non-distal disease were increasing age and male sex, quality and strength of data does not support an individualized biopsy protocol at this time. Finally, in addition to establishing the diagnosis, assessing the distribution of eosinophilia at the time of EoE diagnosis may have implications on management and prognosis. In this study, patients with proximal predominant eosinophilia were less likely to have a histologic response to proton pump inhibitors compared with those with distal predominant eosinophilia, and may provide prognostic information regarding treatment response.

Caution

The study was retrospective and conducted at tertiary care centers, which may limit generalizability. Biopsy site classification relied on endoscopist reporting, and only a minority of patients underwent three-site biopsies, potentially underestimating discordance rates. Selection bias may have influenced which patients received sampling from multiple levels in the esophagus.

My Practice

In my clinical practice, in those patients who I have a suspicion for EoE, I perform biopsies from multiple locations in the esophagus—ideally off PPI therapy. I typically follow current guideline recommendations by routinely sampling the distal and either the proximal or mid esophagus. This study shows that this strategy may miss a meaningful subset of patients with EoE. As a result, I likely will modify my biopsy protocol moving forward and include distal, mid, and proximal esophageal biopsies in all patients with suspected EoE, regardless of endoscopic appearance, to maximize diagnostic yield.

For Future Research

Further studies are needed to determine the utility of characterizing eosinophil distributions and the optimal biopsy protocol for the assessment of EoE. Studies are also needed to define the prognostic and therapeutic implications of eosinophil distribution patterns and to determine the cost-effectiveness of expanded biopsy protocols. Clarifying whether biopsy site selection can potentially guide personalized treatment strategies represents an iportant next step.

Conflict of Interest

The author has no relative conflict of interest.

Abbreviations

EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; eos, eosinophils; hpf, high-power field; PPI, proton pump inhibitor.

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