Eosinophilic gastrointestinal disorders (EGIDs) are diagnosed
• To investigate optimal cutoff values for accurate detection of EoG and EoD
• To explore a single peak hpf threshold indicative of EoG and EoD
• An evidence-based approach to establish appropriate eosinophil enumeration in gastric and duodenal biopsies in some patients with EoG or EoD

Different eosinophil thresholds have been set for diagnosis of EoG and EoD, but there has been no consensus on the criteria.

Eosinophil enumeration in gastric and duodenal biopsies in some studies have required counts of eos in multiple hpf, specifically 5 hpf for EoG and 3 hpf for EoD.

Thresholds requiring multiple hpf may not be practical for routine clinical use.

Figure 2. Representative Images of 5 Non-Overlapping Fields per Specimen as an approach to assessing counts

Statistical Analyses

Area under the receiver operating characteristic (AUROC) curve analysis was performed to identify the best eos cutoff for detection of EoG and EoD

ROC curve evaluates the predictive accuracy of a diagnostic test by calculating its sensitivity and specificity

Sensitivity: proportion of subjects who are correctly categorized as having disease (e.g., EoG) among those who truly have the disease

Specificity: proportion of subjects who are correctly categorized as not having disease among all subjects who truly don’t have the disease

Area under the ROC curve (AUC) of 1.0 indicates that an instrument can discriminate perfectly between active disease and none, whereas a value of 0.5 indicates that an instrument has no discriminating power

Two approaches were used to determine the eos cutoff value analysis relating symptom burden to hpf(s)

Estimate of Youden Index for different threshold points

• Measures biomarker effectiveness and enables the selection of an optimal threshold value (cutoff point) for the marker

Youden Index = Maximum (Sensitivity + Specificity -1)

Index >1 indicates no false negative or false positive rate

Estimate of AUC (Specificity-Specificity) for different threshold points

• Measures the absolute difference between sensitivity and specificity

• Sensitivity, Specificity equality when AUC (Specificity-Specificity) = 0

Determination of Optimal Eosinophil Thresholds for Diagnosis of Eosinophilic Gastritis and Duodenitis: A Pooled Analysis of 4 Prospective Adult Studies

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METHODS

Figure 2. Representative Images of 5 Non-Overlapping Fields per Specimen as an approach to assessing counts

Objectives

Background

• Eosinophilic gastrointestinal disorders (EGIDs) are diagnosed based on a combination of symptoms and elevated numbers of eosinophils (eos) observed in biopsy specimens from esophagus (eosinophilic esophagitis [EoE]), stomach (eosinophilic gastritis [EoG]), and/or upper intestine (eosinophilic duodeni [EoD]).

Figure 1. Pathogenesis of EGIDs

Figure 3. Screening Protocol

Figure 4. Peak and Mean Eosinophil Counts Across 3 Prospective EoG/EoD Trials

Figure 5. ROC Curves for Single Gastric and Single Duodenal HPF

Conclusions/Discussion

• Using multiple hpf, we identified optimal eos counts that correlate with qualifying symptom burden:

- EoG gastric thresholds: 20 eos/hpf and 3 duodenal hpf were 0.78 and 0.74, respectively

- Utilizing AUROC curves and two separate cutoff value analyses, the optimal eos threshold for a single hpf is 33 eos/hpf in 1 gastric hpf for EoG and 37 eos/hpf in 1 duodenal hpf for EoD

- The ROC curve areas relating disease characteristics with eosinophil counts per 1 gastric hpf and 1 duodenal hpf were 0.94 and 0.94, respectively

- Using multiple hpf, we identified optimal eos counts that correlate with qualifying symptom burden:

- EoG gastric thresholds: 20 eos/hpf and 3 duodenal hpf were 0.78 and 0.74, respectively

- Utilizing AUROC curves and two separate cutoff value analyses, the optimal eos threshold for a single hpf is 33 eos/hpf in 1 gastric hpf for EoG and 37 eos/hpf in 1 duodenal hpf for EoD

- These thresholds for EoG and EoD could be used to help develop future practical histopathologic diagnostic guidelines

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- Two approaches were used to determine the eos cutoff value analysis relating symptom burden to hpf(s)

- Estimate of Youden Index for different threshold points

  • Measures biomarker effectiveness and enables the selection of an optimal threshold value (cutoff point) for the marker

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  • Index >1 indicates no false negative or false positive rate

- Estimate of AUC (Specificity-Specificity) for different threshold points

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Figure 4A. Symptoms Across 3 Prospective EoG/EoD Trials

Figure 5A. ROC Curves for 5 Gastric HPFs and 3 Duodenal HPFs

Figure 5B. ROC Curves for Single Gastric and Single Duodenal HPF

Figure 6. Receiver Operating Characteristic (ROC) Curve for Sensitivity and Specificity of Eosinophil Count per HPF

Receiver Operating Characteristic (ROC) Curve for Sensitivity and Specificity of Eosinophil Count per HPF

Mean Tissue Eosinophil Counts

Gastric Mean counts / 3 hpf

Duodenal Mean counts / 3 hpf

EoG Mean counts / 3 hpf

EoD Mean counts / 3 hpf

Duodenal HPF

Gastric HPF

• The ROC curve areas relating disease characteristics with eosinophil counts per 5 gastric hpf and 3 duodenal hpf were 0.78 and 0.74, respectively

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 Shapiro- Wilk Normality Test

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Reference

• Of the biopsy specimens examined, 5 were obtained from areas of greatest eosinophil density used for counting of eosinophils.

• An evidence-based approach to establish appropriate eosinophil thresholds for EoG and/or EoD is needed

• To investigate optimal cutoff values for accurate detection of EoG or EoD using data from 4 prospective studies

• To explore a single peak hpf threshold indicative of EoG and EoD

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