Optimization of Eosinophilic Gastritis/Duodenitis Detection Requires Evaluation of Multiple High-Powered Fields in Each of 8 Gastric and 4 Duodenal Biopsies: Analysis from a Randomized Trial

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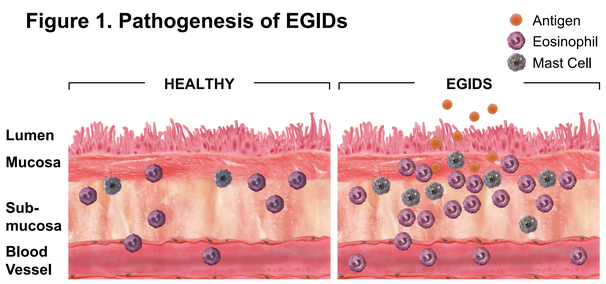
BACKGROUND

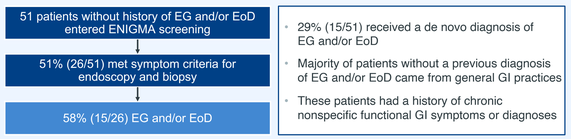
- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in chronic inflammatory diseases in the gastrointestinal (GI) tract, including eosinophilic esophagitis (EoE), gastritis (EG), duodenitis (EoD), and colitis–collectively termed eosinophilic gastrointestinal diseases (EGIDs)[1,2]
- Patients with EGIDs have decreased quality of life due to chronic debilitating and often nonspecific symptoms such as dysphagia, abdominal pain, abdominal cramping, bloating, early satiety, loss of appetite, nausea, vomiting, and diarrhea

Figure 1. Pathogenesis of EGIDs



- ENIGMA was a randomized, controlled, phase 2 trial of adult patients with EG and/or EoD that established the therapeutic potential of lirentelimab–a monoclonal antibody against siglec-8 that depletes eosinophils and inhibits mast cell activity[3]
- Patients enrolled in the ENIGMA study were first screened for moderate–severe GI symptoms
- Patients who met the symptom criteria underwent esophagogastroduodenoscopy (EGD) with biopsy and histopathologic evaluation to confirm diagnoses of EG and/or EoD (≥30 eosinophils per hpf in ≥5 hpfs in gastric biopsies and/or in ≥3 hpfs in duodenal biopsies)
- Among patients enrolled in the ENIGMA study, 45% had no previous diagnoses of EG and/or EoD; 29% of these patients were found to have EG and/or EoD in the study

Figure 2. De Novo EG and/or EoD Diagnosis in ENIGMA



- 29% (15/51) received a de novo diagnosis of EG and/or EoD
- Majority of patients without a previous diagnosis of EG and/or EoD came from general GI practices
- These patients had a history of chronic nonspecific functional GI symptoms or diagnoses

- This high discovery rate of EG and/or EoD, along with other studies reporting underdiagnosis of EG and/or EoD, prompted further evaluation of the screening protocol
- Using screening data from this prospective, multicenter, phase 2, randomized controlled trial, we assessed rates of diagnosis and defined the number of biopsies required to optimize detection of EG and/or EoD

METHODS

Figure 3. Biopsy and Histopathology Protocol and Diagnostic Criteria for EG and/or EoD

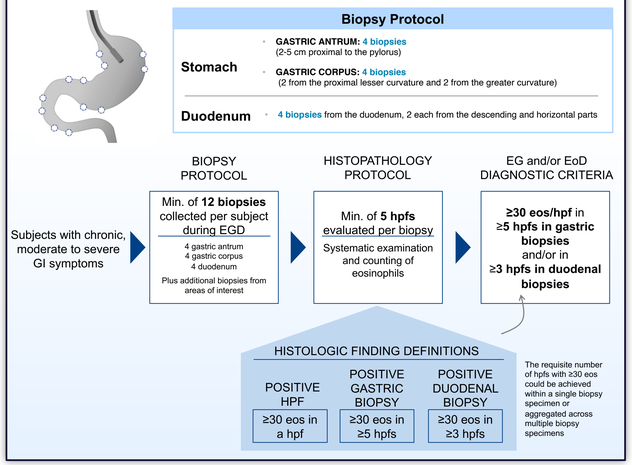


Figure 4. Histopathologic Evaluation Process

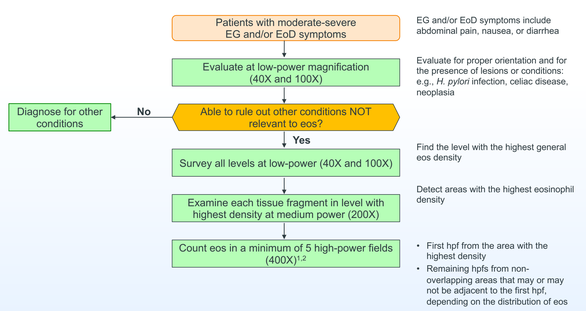
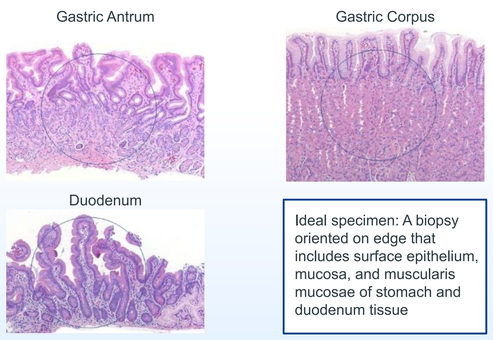


Figure 5. Ideal Biopsy Specimen



RESULTS

Figure 6. EG and/or EoD Diagnosis Rate in Patients

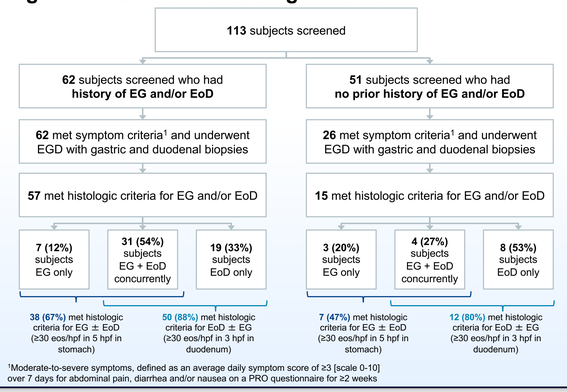


Table 1. Patient Demographics

Patient Characteristics	Met EG and/or EoD Criteria N=72	EG±EoD N=45	EoD w/o EG N=27
Mean age, years (range)	42 (18-74)	41 (18-68)	43 (19-74)
Female sex, n (%)	43 (60%)	25 (56%)	18 (67%)
White, n (%)	66 (92%)	41 (91%)	25 (93%)
Weight, mean (range), kg	82 (47-171)	82 (47-171)	82 (48-119)
Total Symptom Score at baseline, mean ±SD	31 ± 14	33 ± 14	29 ± 13
History of asthma, allergic rhinitis, atopic dermatitis, and/or food allergy	48 (67%)	33 (73%)	15 (56%)
Absolute eosinophil count			
Mean ±SD	654 ± 951	766 ± 1030	467 ± 784
Subjects with ≥250/µl, n (%)	45 (63%)	32 (71%)	13 (48%)
Subjects with ≥500/µl, n (%)	26 (36%)	21 (47%)	5 (19%)
Prior history, n (%)			
Eosinophilic gastritis and/or duodenitis (EG and/or EoD)	57 (79%)	38 (84%)	19 (70%)
Functional gastrointestinal disorder[a]	24 (33%)	13 (29%)	11 (41%)
Gastroesophageal reflux disease (GERD), acid reflux, or heartburn	24 (33%)	16 (36%)	8 (30%)
Peptic ulcer	9 (13%)	8 (18%)	1 (4%)
Chronic gastritis/duodenitis	4 (6%)	1 (2%)	3 (11%)
Physician-guided treatment, n (%)			
Proton pump inhibitor	35 (49%)	22 (49%)	13 (48%)
Diet modification	11 (15%)	6 (13%)	5 (19%)
Low-dose systemic corticosteroid[b]	7 (10%)	5 (11%)	2 (7%)
Topical steroid (budesonide) capsule	7 (10%)	6 (13%)	1 (4%)

[a]Irritable bowel syndrome, functional abdominal pain, functional diarrhea, or functional constipation
[b]Prednisone ≤10mg daily or equivalent as a pre-existing regimen and taken throughout the study

Figure 7. Distribution of Patients With and Without a Prior Diagnosis of EG and/or EoD

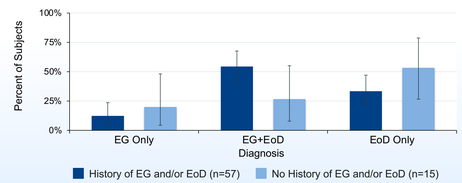
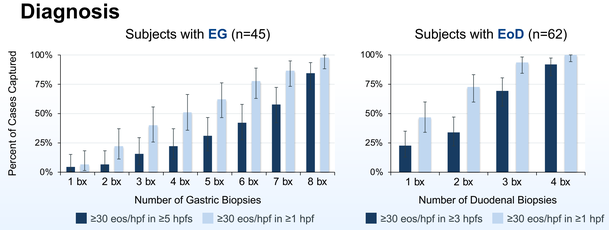


Figure 8. Number of Biopsies Required for EG and/or EoD Diagnosis



- A minimum of 8 gastric and 4 duodenal biopsies are required

Figure 9. Patchiness of Eosinophils in EG and/or EoD Patients

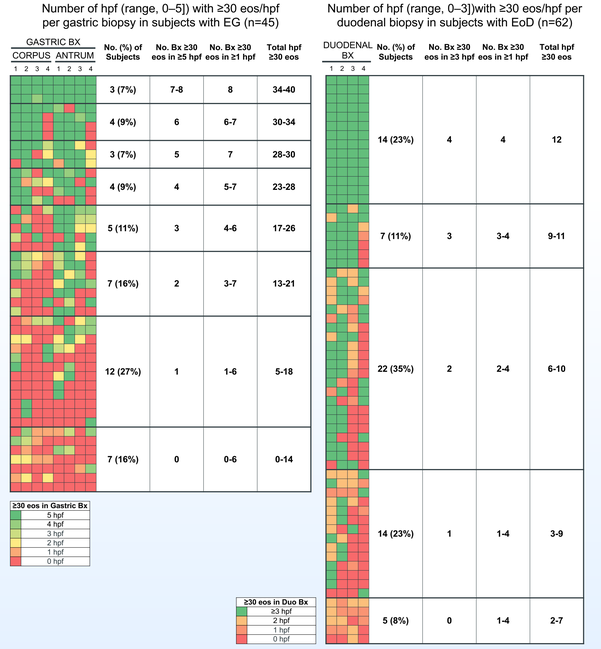
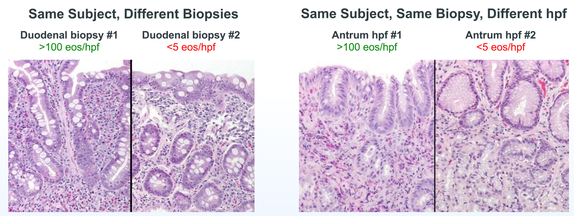


Figure 10. Patchiness of Eosinophils in Tissue



- Due to the patchiness of gastric and duodenal eosinophilia, insufficient biopsy sampling in clinical practice might produce false-negative results and missed diagnoses

CONCLUSIONS/DISCUSSION

- The high detection rate in previously undiagnosed patients and patchiness of gastric and duodenal eosinophilia suggest that a biopsy protocol of a minimum of 8 gastric and 4 duodenal biopsies and quantification of tissue eosinophils will increase EG and/or EoD diagnostic yield
- In contrast to previous reports, EoD was found as frequently as EG, and was also found in some subjects without concomitant eosinophilia of other regions of the GI tract

Reference: (1) Caldwell JM, et al. J Allergy Clin Immunol. 2014.; (2) Youngblood BA, et al. Gastroenterology. 2019.; (3) Dellon ES, et al. NEJM. 2020.

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