Histopathologic Diagnostic Criteria for Eosinophilic Gastritis and Eosinophilic Duodenitis

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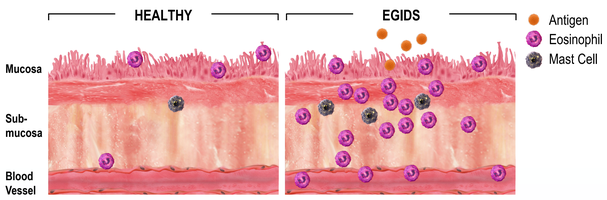
BACKGROUND

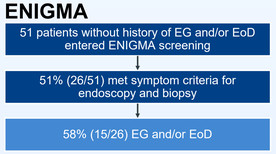
- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in chronic inflammatory diseases in the gastrointestinal (GI) tract, including eosinophilic esophagitis (EoE), gastritis (EG), duodenitis (EoD), and colitis—collectively termed eosinophilic gastrointestinal diseases (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. Patients With New Diagnoses of EG and/or EoD in ENIGMA



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

- This high discovery rate of EG and/or EoD, and reports of underdiagnosis of EG and/or EoD from other studies, prompted further evaluation of the screening protocol
- Using screening data from this prospective, multicenter, phase 2, randomized controlled trial, we assessed rates of EG and/or EoD diagnosis and eosinophilia in 8 gastric and 4 duodenal biopsies from each patient

METHODS

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

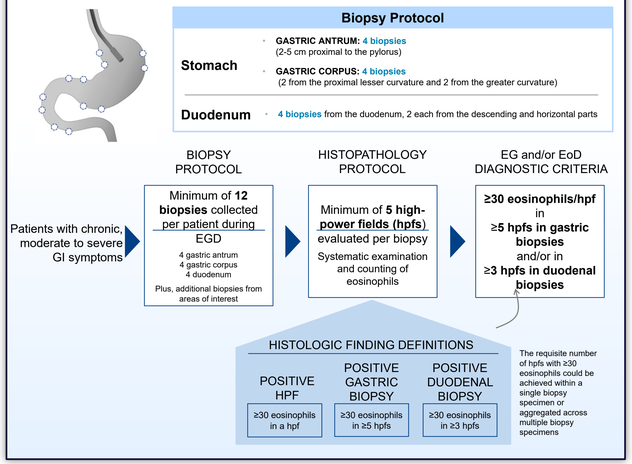
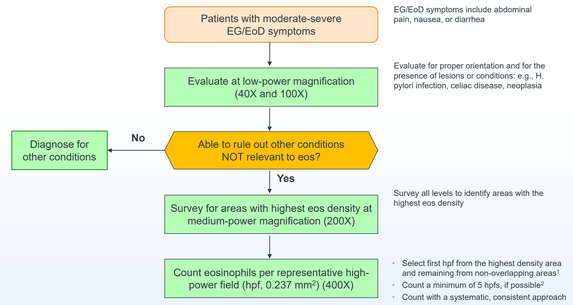
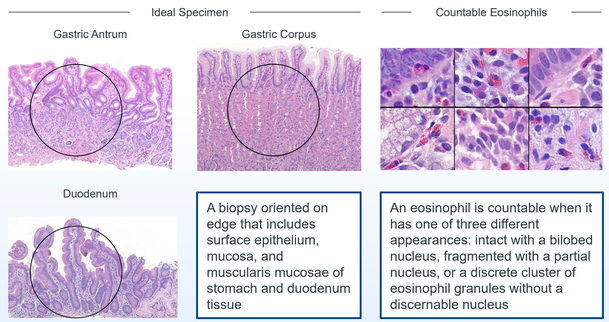


Figure 4. Histopathologic Evaluation Process



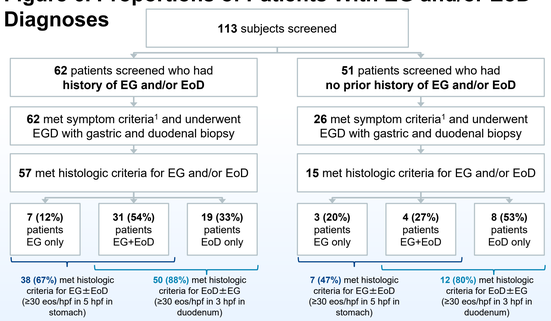
1 Non-overlapping hpfs could be, but are not required to be, adjacent to the first hpf, depending on the distribution of eosinophils in the specimen
2 If the size of a specimen is insufficient to evaluate 5 independent fields, eosinophils are to be counted in as many non-overlapping fields as available

Figure 5. Ideal Biopsy Specimen & Countable Eosinophils



RESULTS

Figure 6. Proportions of Patients With EG and/or EoD Diagnoses



[1]Moderate–severe symptoms, defined as an average daily symptom score of ≥3 (scale 0-10) over 7 days for abdominal pain, diarrhea, and/or nausea on a patient-reported outcome questionnaire for ≥2 weeks

Table 1. Patient Demographics

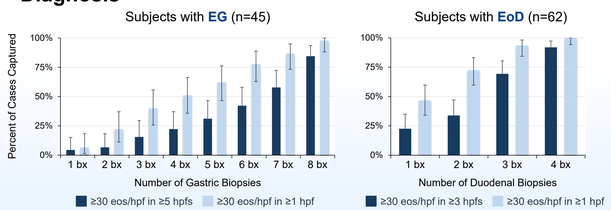
Patient Characteristics	Met EG and/or EoD Criteria n=72	EG±EoD n=45	EoD w/o EG n=27
Mean age, years (range)	42 (18-74)	41 (19-68)	43 (19-74)
Female sex, n (%)	43 (60%)	25 (56%)	18 (67%)
White, n (%)	66 (92%)	41 (91%)	25 (93%)
Weight, mean (range), kg	82 (47-171)	82 (47-171)	82 (48-119)
Total symptom 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

Table 2. Proportion of hpfs With ≥30 Eos in Gastric and Duodenal Biopsies

# hpfs with ≥30 Eosinophil Counts	Gastric Biopsies in 45 Patients w/ EG	Duodenal Biopsies in 62 Patients w/ EoD	All Biopsies
Total Biopsies	329	230	559
0 hpfs	120 (36%)	29 (13%)	149 (27%)
1 hpf	16 (5%)	23 (10%)	39 (7%)
2 hpfs	23 (7%)	38 (17%)	61 (11%)
3 hpfs	20 (6%)	30 (13%)	50 (9%)
4 hpfs	24 (7%)	26 (11%)	50 (9%)
5 hpfs	126 (38%)	84 (37%)	210 (38%)

Figure 7. Number of Biopsies Required for EG and/or EoD Diagnosis



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

Figure 8. Patchiness of Eosinophils in Patients With EG and/or EoD

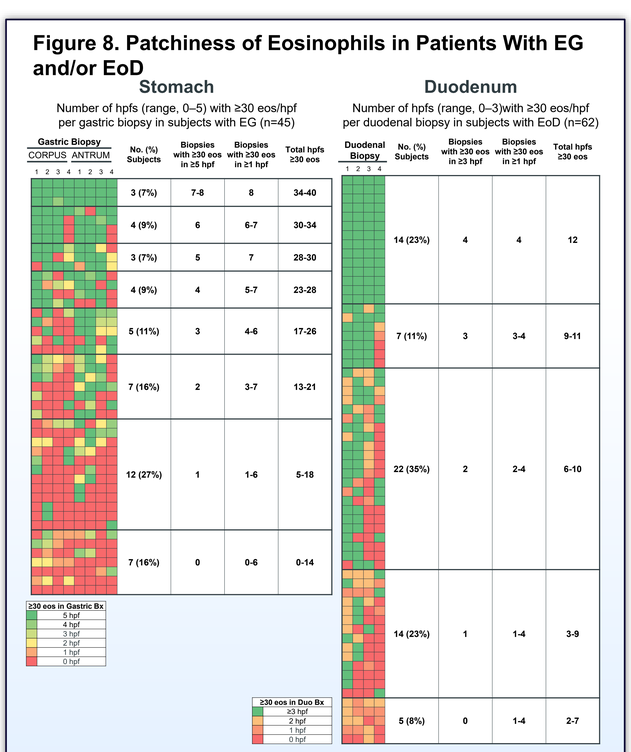
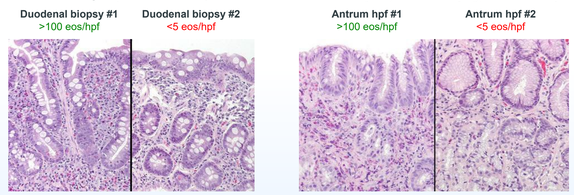


Figure 9. Patchiness of Eosinophils in Tissue



- Due to the patchiness of gastric and duodenal eosinophils, collection of an insufficient number of biopsies in practice might produce false-negative results and missed diagnoses

CONCLUSIONS/DISCUSSION

- There are no consensus diagnostic guidelines for EG and/or EoD; clinical trials use diagnostic criteria of ≥30 eosinophils per hpf in 5 hpfs in gastric biopsies for EG and in 3 hpfs in duodenal biopsies for EoD
- Evaluation of at least 12 biopsies, at high power, in ≥5 hpfs, is required to ensure detection of EG and/or EoD
- Application of this histopathology protocol to clinical practice may increase diagnosis of EG and/or EoD

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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