

# Gastroduodenal Eosinophilia Is Under-Appreciated in Eosinophilic Esophagitis (EoE) Patients With Functional Bowel Symptoms: A Real Life Experience

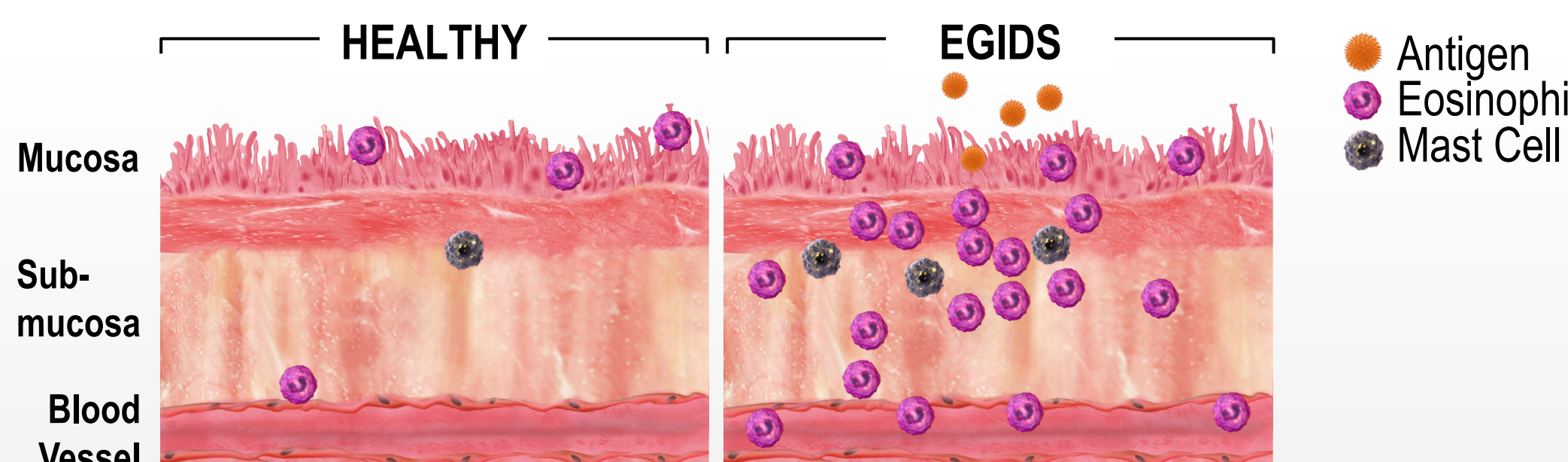
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## BACKGROUND

- Eosinophilic gastrointestinal (GI) disorders are chronic inflammatory conditions characterized by the aberrant localized accumulation and activation of eosinophils and mast cells<sup>1,2</sup>
- Eosinophilic esophagitis (EoE) is the best understood of these disorders, but there is evidence that eosinophilic gastritis and/or duodenitis (EG/EoD) are more prevalent than previously thought
- Many patients with EoE have extra-esophageal GI symptoms that are unlikely to be caused by inflammation limited to the esophagus
- These patients may have EG and/or EoD, which are missed if gastric and duodenal biopsies are not systematically collected and evaluated for eosinophils

Figure 1. Pathogenesis of EGIDs



- EG and EoD are thought to affect 45,000–50,000 patients in the US, although there is evidence that these disorders are more common
- Current treatment options such as diet restriction and corticosteroids have limited efficacy and/or are inappropriate for chronic use
- New therapies are needed

## OBJECTIVE

- We evaluated gastric and duodenal biopsies from patients with EoE, with and without persistent non-esophageal GI symptoms, to determine the frequency of EG and/or EoD in these patients

## METHODS

- We recruited patients with EoE previously evaluated by esophagogastroduodenoscopy (EGD) and whose gastroduodenal biopsies were reported to be normal or have non-specific inflammation
- Patients were grouped by presence or absence of extra-esophageal symptoms:
  - We identified 52 EoE patients with extra-esophageal GI symptoms (abdominal pain, nausea, bloating, and/or irritable bowel syndrome [IBS]) who had stomach and small bowel biopsies interpreted as non-specific inflammation—this group was called EoE+S
  - 15 EoE patients without extra-esophageal GI symptoms were included as a control group, called EoE–S
- Biopsies taken at the initial evaluation were stained with hematoxylin and eosin and evaluated by a blinded, central pathologist for eosinophil counts and morphology
- We also collected data on endoscopic features and functional gastrointestinal symptoms

## RESULTS

- After excluding patients with gastric or duodenal surgeries, opiate dependence, systemic immunosuppression, *H Pylori*, or loss of tissue, we evaluated 45 EoE+S patients and 12 EoE–S patients
- Common symptoms among EoE+S patients were abdominal pain, bloating, nausea, and IBS
- EoE+S patients had undergone as many as 6 tests, in addition to EGD, to evaluate their extra-esophageal symptoms
- All patients had prior pathology reports of non-specific inflammation or normal tissue
- Our blinded re-assessment of biopsies found that:
  - many EoE+S patients met histologic criteria for EG/EoD:
    - 8/45 (18%) had EG ( $\geq 30$  eos/hpf in  $\geq 5$  gastric hpfs)
    - 23/45 (51%) had EoD ( $\geq 30$  eos/hpf in  $\geq 3$  duodenal hpfs)
    - 7/45 (16%) had concomitant EG and EoD
  - None of the EoE–S patients met histologic criteria for EG
    - 3/12 (25%) EoE–S patients met histologic criteria for EoD
- EG±EoD, EoE+S patients had peak eosinophil counts of  $58 \pm 14$  in gastric biopsies
- EoD ±EG, EoE+S patients had peak eosinophil counts of  $57 \pm 19$  in duodenal biopsies
- EoE–S patients had peak counts of  $11 \pm 7$  in gastric and  $35 \pm 21$  in duodenal biopsies

Table 1. Baseline Characteristics of EoE Patients

Patient Characteristics	With Symptoms (EoE+S) n=45	Without Symptoms (EoE–S) n=12
Age, years	34.1±11.1	40.4±15.4
Male sex	49%	67%
Initial gastric pathology		
Normal	62%	83%
Nonspecific inflammation <sup>a</sup>	38%	17%
Initial duodenal pathology		
Normal	91%	100%
Nonspecific inflammation	9%	0
Types of additional tests performed <sup>b</sup>	3±2	0
Final diagnosis		
Eosinophilic gastritis (EG)	18% <sup>c</sup>	0
Eosinophilic duodenitis (EoD)	51%	25%
EG and EoD	16%	0
Peak esophageal eosinophils	41.1±36.2	51.7±28.6
Peak gastric eosinophils	25.9±21.1	11.1±6.5
Peak duodenal eosinophils	43.1±20.8	35.2±21.0
EREFS	2.7±2.0	3.9±1.4

Values reported as mean ± standard deviation or proportion of patients  
<sup>a</sup> Includes reactive gastritis, chronic gastritis, focal inflammation, duodenitis, reactive epithelial changes  
<sup>b</sup> Additional EGDs with biopsies for pain, breath tests for bacterial overgrowth, colonoscopies, capsule endoscopies, exploratory laparoscopy, ultrasound, computed tomography, single-balloon enteroscopy, etc  
<sup>c</sup> 7/8 were diagnosed with nonspecific inflammation of the stomach

Figure 2. Functional GI Symptoms Present in EoE Patients

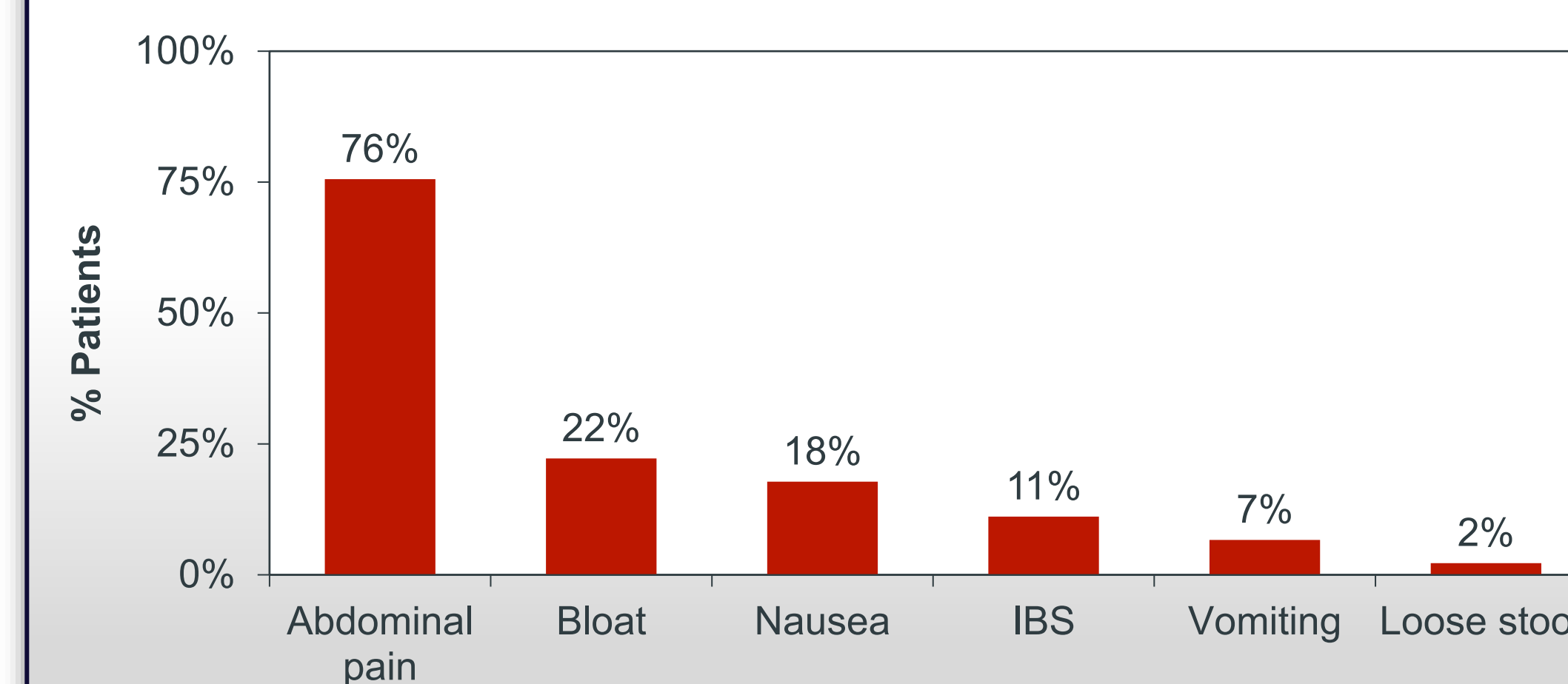


Figure 3. Gastric and Duodenal Morphologic Features of EoE Patients With and Without GI Symptoms

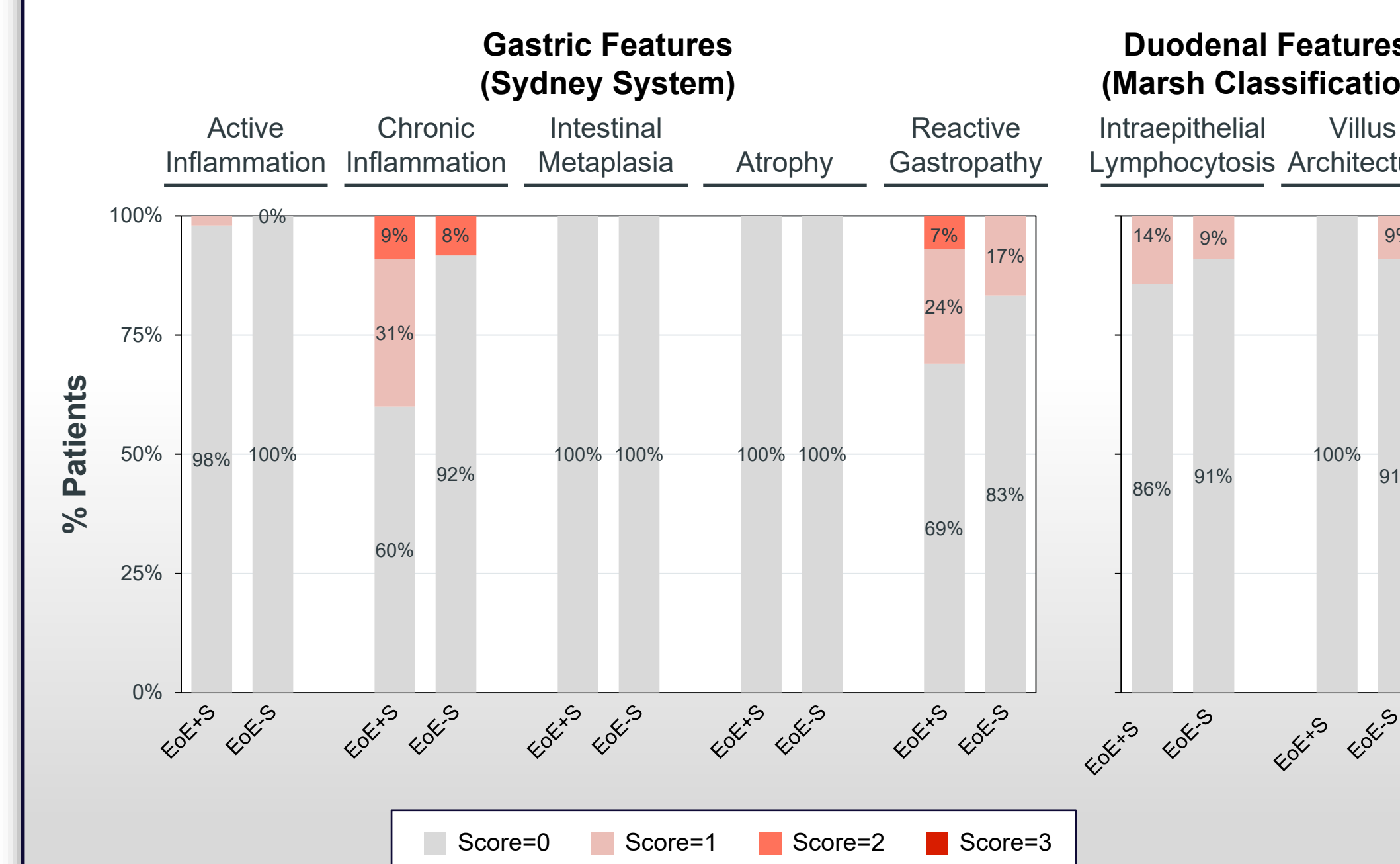
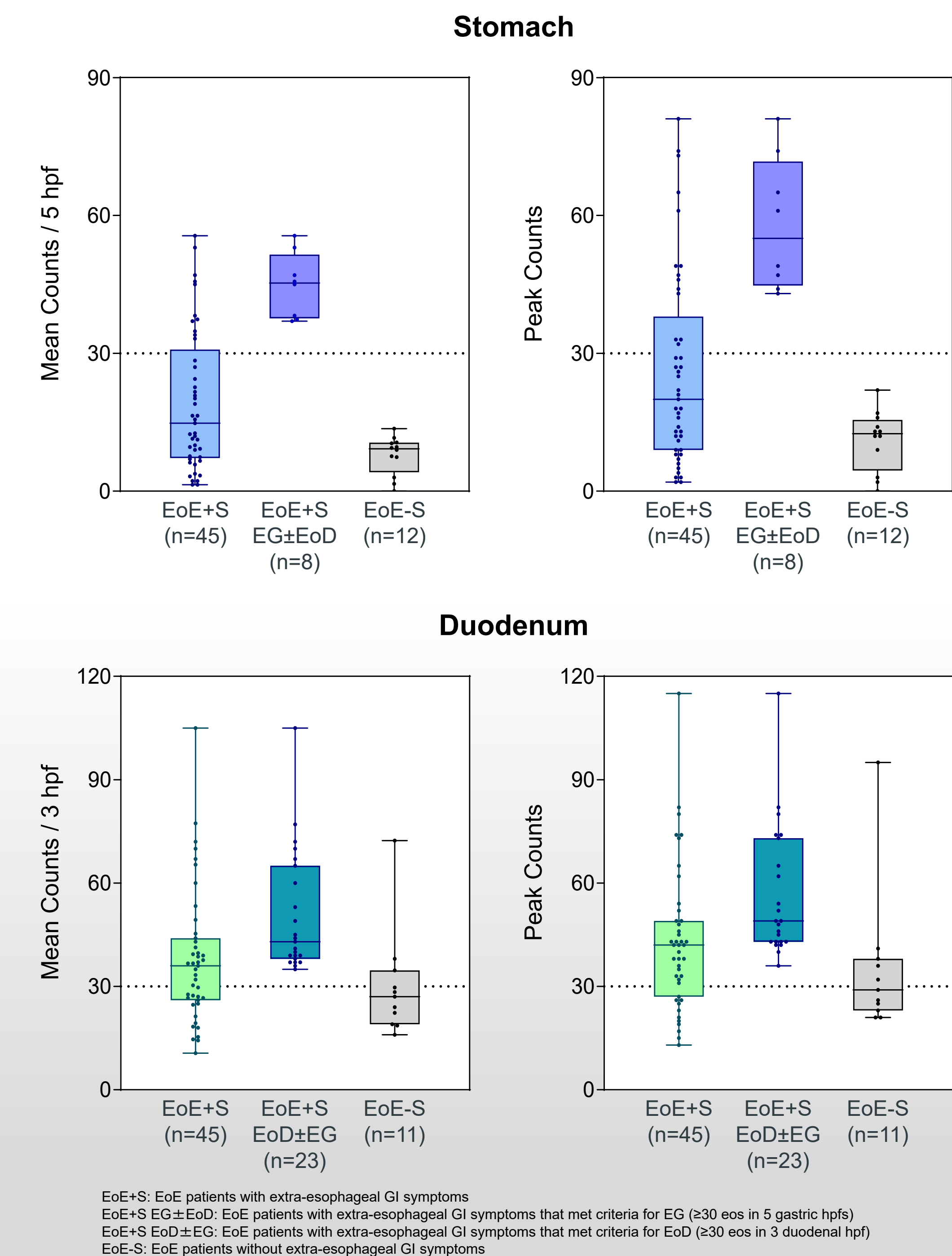


Figure 4. Mean and Peak Eosinophil Counts in EoE Patients With and Without GI Symptoms



EoE+S: EoE patients with extra-esophageal GI symptoms  
 EoE+S EG±EoD: EoE patients with extra-esophageal GI symptoms that met criteria for EG ( $\geq 30$  eos in 5 gastric hpfs)  
 EoE+S EoD±EG: EoE patients with extra-esophageal GI symptoms that met criteria for EoD ( $\geq 30$  eos in 3 duodenal hpfs)  
 EoE–S: EoE patients without extra-esophageal GI symptoms

## CONCLUSIONS/DISCUSSION

- In patients with EoE and extra-esophageal GI symptoms (EoE+S), review of gastric and duodenal biopsies previously reported to be normal or have non-specific inflammation revealed that many patients have EG and/or EoD, based on histologic criteria
- These findings indicate that gastric and duodenal eosinophils should be counted in patients with EoE and persistent non-esophageal GI symptoms
- Increased awareness of EG and/or EoD and consensus diagnostic criteria may lead to identification of undiagnosed patients with EG and/or EoD
- Proper diagnosis of EG and/or EoD could lead to targeted treatment of gastric and/or duodenal inflammation and symptoms