

Eosinophilic Esophagitis Histology Scoring System (EoE HSS) Form affects function

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EoE HSS pathology indicates numerous types of abnormalities

- The features significantly correlate with clinical signs and symptoms, and with the macroscopic features of the disease, to varying degrees.
- The features also relate to underlying pathogenetic mechanisms.
- Correlations with clinical metrics have been emphasized, but relationships with mechanisms have not.
- Following are some mechanistic analyses of the EoE HSS features.

Implications of EoE HSS features

- Eosinophil inflammation can be chronic, meaning of prolonged duration (as opposed to infiltration by lymphocytes), and chronicity is associated with increased risk of malignancy in the GI tract (IBD has increased cancer risk).
 - Oncology 2002;16(2):217-226
 - Eosinophil infiltration in CRC (increasing in incidence) is associated with decreased mortality.
 - Mod Pathol 2016;29:516-527
 - Increased circulating proinflammatory substances promote diseases.
 - Nature 2006;444(Dec):860-867
- Basal zone hyperplasia results from increased cell proliferation, in biopsies with or without eosinophils, which increases the risk of errors in copying genes (sometimes visible as abnormal mitotic figures), and increases the reservoir of cells producing eotaxin-3.
 - J Pediatr Surg 2020;55:2144-2149
 - World J Gastroenterol 2019;25(7):870-879
 - J Allergy Clin Immunol 2007;120:1292-1300

Implications of EoE HSS features

- Eosinophil abscess is an accumulation of eosinophils in an area devoid of underlying architecture. Usually small, eosinophil abscess in esophageal squamous epithelium may also be very large and numerous, especially along the surface predisposing to ulcer.
 - Allergy Asthma Clin Immunol 2019;15:12
- Eosinophil surface layering is a term used to describe the linear distribution of eosinophils in the upper third of esophageal epithelium, and the periglandular collars seen in eosinophilic gastritis may be related. This may result from communication with luminal contents.
 - Gastroenterology 2002;122:1216-1225

Implications of EoE HSS features

- Dilated intercellular spaces correlate with abnormal mucosa impedance at the biopsy site, and increased intraepithelial food antigen, consistent with impaired mucosal integrity.
 - Clin Gastroenterol Hepatol 2015;13:1242-1248
 - Aliment Pharmacol Ther 2017;45:427-433
- Surface epithelial alteration, first described in GERD, may be a protective reaction that alters transepithelial permeability.
- Dyskeratotic epithelial cells are considered a manifestation of mucosal injury in lymphocytic esophagitis, a disorder that may be found in patients who have esophageal dysmotility, GERD, and immune-mediated diseases.
 - Ann NY Acad Sci 2018;1434:185-191

Implications of EoE HSS features

- Surface epithelial alteration and dyskeratotic epithelial cells strongly predict the presence of lamina propria fibrosis in esophageal biopsies from children who have EoE.
 - Clin Gastroenterol Hepatol 2020 doi: 10.1016/j.cgh.2020.07.035
- Lamina propria fibrosis may indicate reversible or potentially nonreversible connective tissue change.
 - J Allergy Clin Immunol 2016;137:147-156
 - J Gastroenterol 2019;54:10-18

EoE severity

- All or most of these features may be considered severe, and are graded and staged for magnitude of change in the EoE HSS.
- EoE is a clinicopathologic disease, and a severity score therefore must include pathology metrics.
- Data concerning abbreviated metrics to define severity do not exist.

Histologic evaluation of severity in GERD

- Basal zone hyperplasia, papillary elongation, dilated intercellular spaces, and peak count of intraepithelial eosinophils were used to compose a severity score.
- Those features were found to be the most informative, and presence of lymphocytes and neutrophils were not.
- Evaluated features did not include eosinophil abscess, surface layering, surface epithelial alteration, dyskeratotic epithelial cell, or lamina propria fibrosis.
- Maximum score for each of 4 features was 2; the total was divided by the number of features assessed for a total severity score.
- Score of 1 or higher was considered severe.
 - Hum Pathol 2014;45:994-1002

Abbreviated histologic evaluation of severity in EoE

- Eosinophil inflammation is critical for diagnosis and for evaluation of active vs not active disease, and should be included.
- Basal zone hyperplasia is a common feature, with clinical and functional sequelae.
- Dilated intercellular spaces virtually always accompany basal zone hyperplasia; the exception is inactive post-therapy biopsies which are not likely to be the histology of EoE severity. Therefore including dilated intercellular spaces along with basal zone hyperplasia is unnecessary.

Abbreviated histologic evaluation of severity in EoE

- For subjects with endoscopically confirmed stricture, evaluation of the lamina propria is superfluous.
- For all other subjects, evaluation for fibrosis could indicate current and future severity requiring intervention.
- If lamina propria is not present, or ***too crushed to evaluate***, surface epithelial alteration, and/or dyskeratotic epithelial cells should be evaluated, and the presence of both or either considered strong indicators of the likelihood that lamina propria fibrosis is present.
 - Clin Gastroenterol Hepatol 2020 doi: 10.1016/j.cgh.2020.07.035

Abbreviated histologic evaluation of severity in EoE

- The advantages of short, simple checklists include reduced time to determine an important clinical metric for clinicians whose practice does not consist largely of EoE patients.
- The advantages of including EoE HSS features include encouraging communication between clinician and pathologist which virtually always improves patient care.
- The disadvantages include loss of important metrics including evaluating the extent of pathologic changes.