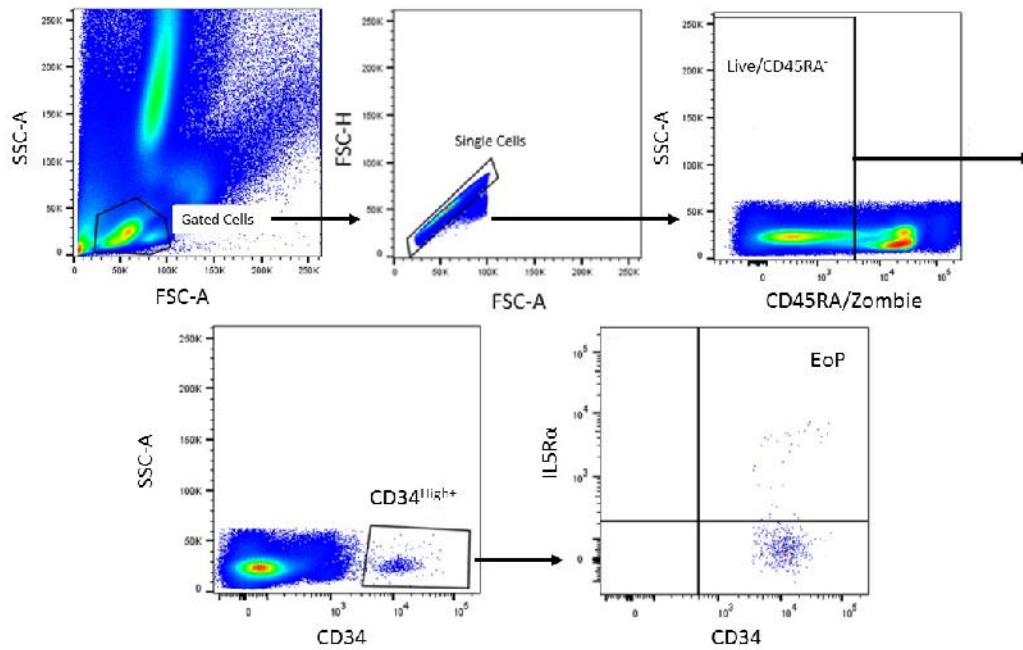


SDC 1: Whole blood staining method and gating strategy for EoPs.



The blood was washed and blocked with dilute fetal bovine serum prior to antibody staining. Blood was stained with CD45RA-APC-Cy7 (BioLegend, clone H1100), CD125-PE (BD Bioscience, Lot 7355839), CD34-BV421 (BioLegend, clone 561), and Zombie NiR fixable viability kit. The cells were then fixed and lysed with BD FACS lysis solution, washed with PBS, and stored overnight in 1% formaldehyde at 4°C. Flow cytometry was performed the following day. All data were acquired on BD FACSCanto II analyzer that is maintained by the Research Flow Cytometry Core at Cincinnati Children's Hospital Medical Center. Data were compensated and analyzed using FlowJo software (Tree Star, Ashland, OR). Compensation was calculated in FlowJo using unstained and stained cells (Live/Dead) and OneComp eBeads (eBioscience). Gate boundaries and shapes were determined using fluorescence minus one (FMO) controls, including appropriate isotype antibodies. EoPs are identified in the cell population with low SSC and FSC. Single, live CD45RA⁻ cells were gated for CD34^{high+} events. This population was gated for CD125 (IL-5 receptor α), with double-positive events being considered EoPs. EoP levels are expressed as EoP events per 10⁶ gated events.

SSC, side scatter; FSC, forward scatter.

SDC 2: Comparison of clinical characteristics: included versus excluded samples.

| Characteristic | Included | Excluded | <i>P</i> value |
|--|------------------|------------------|-----------------------|
| N | 34 | 34 | 1.00 |
| Active EoE Disease*, n (%) | 16 (47.1%) | 12 (36.4%) | 0.32 |
| Male, n (%) | 27 (79.4%) | 28 (82.4%) | 0.75 |
| White race, n (%) | 33 (97.0%) | 34 (100%) | 0.31 |
| History of Asthma, n (%) | 12 (35.3%) | 11 (32.3%) | 0.80 |
| History of Atopic Dermatitis, n (%) | 25 (73.5%) | 20 (58.8%) | 0.20 |
| History of Allergic Rhinitis, n (%) | 21 (61.8%) | 21 (61.8%) | 1.00 |
| History of IgE mediated food allergy, n (%) | 21 (61.8%) | 17 (50.0%) | 0.32 |
| AEC, K/mcL, median (IQR) | 0.20 (0.15-0.51) | 0.25 (0.11-0.40) | 0.26 |
| Total IgE, IU/mL, median (IQR) | 201 (35.5-345.8) | 186 (66-342.5) | 0.71 |

*Active EoE defined as esophageal eosinophilia 15eos/HPF

AEC, absolute eosinophil count

IgE, immunoglobulin-E

SDC 3: Spearman correlation between EoP level and EoEHSS components

| Variable | | Spearman | P value |
|-----------------------------|-------------------------------------|----------|--------------|
| HSS stage, composite | | 0.40 | 0.02 |
| HSS grade, composite | | 0.40 | 0.02 |
| Distal Grade | HSS distal grade, combined | 0.41 | 0.02 |
| | Basal zone hyperplasia | 0.36 | 0.04 |
| | PEC | 0.31 | 0.08 |
| | Abscesses | 0.33 | 0.055 |
| | Surface layering | 0.19 | 0.28 |
| | DIS | 0.12 | 0.48 |
| | Lamina propria fibrosis | 0.34 | 0.05 |
| Distal Stage | HSS distal stage, combined | 0.42 | 0.01 |
| | Basal zone hyperplasia | 0.47 | 0.005 |
| | PEC | 0.34 | 0.05 |
| | Abscesses | 0.33 | 0.056 |
| | Surface layering | 0.17 | 0.33 |
| | DIS | 0.32 | 0.06 |
| | Lamina propria fibrosis | 0.31 | 0.07 |
| Proximal Grade | HSS proximal grade, combined | 0.42 | 0.01 |
| | Basal zone hyperplasia | 0.34 | 0.05 |
| | PEC | 0.28 | 0.11 |
| | Abscesses | 0.12 | 0.50 |
| | Surface layering | 0.17 | 0.34 |
| | DIS | 0.17 | 0.33 |
| | Lamina propria fibrosis | 0.25 | 0.15 |
| Proximal Stage | HSS proximal stage, combined | 0.42 | 0.01 |
| | Basal zone hyperplasia | 0.31 | 0.08 |
| | PEC | 0.30 | 0.09 |
| | Abscesses | 0.11 | 0.53 |
| | Surface layering | 0.16 | 0.37 |
| | DIS | 0.20 | 0.25 |
| | Lamina propria fibrosis | 0.25 | 0.16 |

Spearman correlation test for non-parametric data

Composite, combined proximal and distal scores

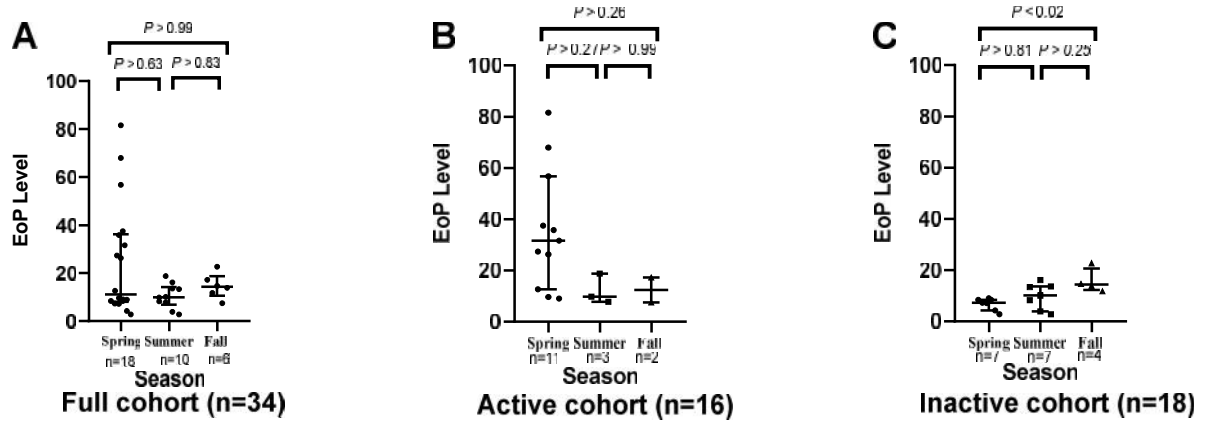
EoEHSS, EoE histologic scoring system

SDC 4: EoP levels in participants with and without co-morbid atopic disease history.

| Characteristic | Yes Median (IQR) | No Median (IQR) | <i>P</i> value |
|---|-----------------------------|----------------------------|-----------------------|
| History of Atopy | 11.7 (8.3 – 18) | 31.6 (3.4-59.5) | 0.64 |
| History of Allergic Rhinitis | 12.7 (8.1 – 18.0) | 11.7 (7.7 – 34.6) | 0.89 |
| History of Atopic Dermatitis | 10.1 (8.0-27.7) | 16.2 (6.4-34.5) | 0.42 |
| History of IgE Mediated Food Allergy | 12.7 (8.0 - 20.7) | 11.7 (8.0 – 56.8) | >0.99 |
| History of Asthma | 13.0 (7.2-15.8) | 10.9 (8.4-28.4) | 0.36 |

Data are expressed as median and IQR and significance determined by Mann-Whitney for pairwise comparisons. IQR: interquartile range (25th-75th%ile)

SDC 5: EoP level by season of sample collection in (A) full cohort, (B) active EoE disease cohort, and (C) inactive EoE disease cohort.



Data are expressed as median and IQR and significance determined by Mann-Whitney for pairwise comparisons and Kruskal-Wallis for multiple comparisons. Circles represent individual samples. *Spring*, March-May; *Summer*, June-August; *Fall*, September-October; *IQR*: interquartile range (25th-75th%ile)

SDC 6: EoP levels do not vary by medication use.

| Characteristic | | Yes Median (IQR) | No Median (IQR) | P value |
|-------------------|---------------|---------------------|--------------------|---------|
| PPI use | | 13.6 (7.8 – 31.6) | 9.7 (8.2 – 17.3) | 0.30 |
| Antihistamine Use | | 9.8 (7.6 – 20.7) | 13.6 (8.3 – 26.8) | 0.61 |
| Steroid Use | | 9.8 (7.8 – 18.7) | 12.7 (8.2– 27.3) | 0.64 |
| Active EoE | PPI | 29.5 (12.0 – 45.1) | 13.5 (8.7 – 33.9) | 0.18 |
| | Antihistamine | 11.3 (8.8 – 41.0) | 29.5 (24 – 48.5) | 0.12 |
| | Steroids | 18.7 (8.8 – 47.1) | 27.3 (9.7 – 37.5) | 0.74 |
| Inactive EoE | PPI | 8.4 (5.7 – 14.1) | 9.0 (6.1 – 12.8) | >0.99 |
| | Antihistamine | 8.4 (4.2 – 14.6) | 9.0 (7.1 – 13.6) | >0.99 |
| | Steroid | 8.4 (6.2 – 13.8) | 9.5 (4.9 – 13.8) | 0.89 |

Data are expressed as median and IQR and significance determined by Mann-Whitney for pairwise comparisons. *PPI*, proton pump inhibitor; *Steroid*, inhaled, intranasal, or topical steroids; *IQR*: interquartile range (25th-75th%ile)

SDC 7: Spearman correlation between disease activity and EoE Endoscopic Reference Score (EREF) components.

| Esophageal site | Endoscopic Finding | EoE Disease Activity by eos/HPF | | EoE Disease Activity by EoP Level (full cohort cut-off of 17) | |
|-----------------|------------------------|---------------------------------|--------------------|---|---------------|
| | | Spearman 95% CI | P value | Spearman 95% CI | P value |
| Proximal | Edema | 0.29 (-0.08-0.59) | 0.12 | 0.31 (-0.06-0.6) | 0.09 |
| | Rings | 0.19 (-0.19-0.52) | 0.31 | 0.26 (-0.11-0.57) | 0.15 |
| | Exudates | 0.46 (0.11-0.70) | < 0.01 | 0.28 (-0.09-0.59) | 0.13 |
| | Furrows | 0.46 (0.11-0.70) | 0.01 | 0.24 (-0.13-0.56) | 0.19 |
| | Total, proximal | 0.43 (0.08-0.69) | 0.02 | 0.31 (-0.06-0.60) | 0.09 |
| Distal | Edema | 0.58 (0.27-0.77) | < 0.001 | 0.37 (0.01-0.65) | 0.04 |
| | Exudates | 0.58 (0.27-0.78) | < 0.001 | 0.41 (0.05-0.68) | 0.02 |
| | Furrows | 0.57 (0.26-0.77) | < 0.001 | 0.40 (0.05-0.67) | 0.02 |
| | Total, distal | 0.65 (0.37 – 0.82) | < 0.0001 | 0.46 (0.12-0.70) | 0.0085 |

Spearman correlation test for non-parametric data

If endoscopic findings not shown, no samples had such finding

Disease activity by eos/HPF: active: 15 eos/HPF

SDC 8: Percent of EoP events that are H1R positive.

| Sample | H1R positive, EoP events (%) | EoE Disease Activity | Antihistamine use |
|---------------|-------------------------------------|-----------------------------|--------------------------|
| 1 | 74.3 | Active | No |
| 2 | 53.3 | Inactive | No |
| 3 | 5.9 | Inactive | No |
| 4 | 22.2 | Inactive | No |
| 5 | 10.0 | Inactive | No |
| 6 | 7.7 | Inactive | Yes |
| 7 | 0 | Inactive | No |
| 8 | 41.2 | Inactive | Yes |
| 9 | 60.0 | Active | Yes |
| 10 | 100.0 | Inactive | Yes |
| 11 | 23.8 | Active | Yes |

H1R, Histamine-type1 receptor