

Validation of the diagnosis of eosinophilic esophagitis based on histopathology reports in Sweden

SUPPLEMENTARY MATERIAL

Laboratory data

Laboratory measures within 3 months from the biopsy were available in 24% of the 111 patients. Hospitals often have different normal ranges for laboratory values. The reference values comes from Orebro University Hospital and are representative of other Swedish hospitals.

White blood cell count varied from 4.2 to $15.1 \times 10^9/l$ (median 7.3) (Reference=3.5–8.8 $10^9/L$). Number of blood eosinophils reported in five patients was 0.1-0.4 and in one patient 3.2 (this latter patient was later diagnosed with hypereosinophilic syndrome (this latter patient also had Barret's esophagus and was not regarded as having EoE) (Reference ≤ 0.6 cell/mL). C-reactive protein was noted in 16 patients (median: 16 mg/L, range: <1-78) (Reference <4mg/L) . Erythrocyte sedimentation rate was registered in four patients (4%) (range 2-16 mm/h) (Reference <20mm/h).

Table S1. Variables examined in the charts of patients with suspected eosinophilic esophagitis (EoE)

Symptoms	Radiology	Endoscopy	Laboratory data
Feeding difficulties	Radiology type	Date of first endoscopy	ESR
Vomiting	Radiology reports	Endoscopy notes	White blood cells
Abdominal pain	Manometry	Date of first biopsy	Serum eosinophils
Weight loss	pH registration	Histopathology report	CRP
Dysphagia		Number of upper biopsies of the esophagus	
Food impaction		Number of lower biopsies of the esophagus	
Other pain		Date of diagnosis	
Eating slowly		EoE listed in patient chart	
		Follow-up biopsy	
		Dilatation	
Allergic diseases	Other diseases	Treatment	Other
Asthma	<i>Helicobacter pylori</i>		Smoking
Allergic rhinitis	<i>Giardia</i>		Alcohol
Atopic dermatitis/ eczema			Body mass index at first biopsy
Confirmed food allergy			Heredity for other diseases

Table S2: Comparison of true versus false EoE for most common symptoms

Symptom	All patients (n=111)	Patients with true EoE (n=99)	Patients with false-positive EoE (n=12)	p-value
Dysphagia, n (%)	78 (70)	71 (72)	7 (58)	0.336
Food impaction, n (%)	64 (58)	61 (62)	3 (25)	0.015
Feeding difficulties, n (%)	37 (33)	33 (33)	4 (33)	1.00
Vomiting, n (%)	19 (17)	19 (19)	0 (0)	
Abdominal pain, n (%)	17 (15)	15 (15)	2 (17)	1.00
Weight loss, n (%)	12 (11)	10 (10)	2 (17)	0.616

Comparing patients with true EoE vs. those with false-positive EoE (not confirmed through patient chart review) revealed that food impaction ($p=0.015$) was significantly more common in true-positive EoE.

References

1. Attwood SE, Smyrk TC, Demeester TR, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci.* 1993;38:109-16.
2. Straumann A, Spichtin HP, Bernoulli R, Loosli J, Vogtlin J. [Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings]. *Schweiz Med Wochenschr.* 1994;124:1419-29.
3. Dellon ES, Hirano I. Epidemiology and Natural History of Eosinophilic Esophagitis. *Gastroenterology.* 2018;154:319-32 e3. doi:10.1053/j.gastro.2017.06.067
4. Lucendo AJ, Molina-Infante J, Arias A, von Arnim U, Bredenoord AJ, Bussmann C, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J.* 2017;5:335-58. doi:10.1177/2050640616689525
5. Miehlke S. Clinical features of eosinophilic esophagitis. *Dig Dis.* 2014;32:61-7. doi:10.1159/000357011
6. Spergel JM, Dellon ES, Liacouras CA, Hirano I, Molina-Infante J, Bredenoord AJ, et al. Summary of the updated international consensus diagnostic criteria for eosinophilic esophagitis: AGREE conference. *Ann Allergy Asthma Immunol.* 2018;121:281-4. doi:10.1016/j.anai.2018.05.035
7. Cheng E, Souza RF, Spechler SJ. Eosinophilic esophagitis: interactions with gastroesophageal reflux disease. *Gastroenterol Clin North Am.* 2014;43:243-56. doi:10.1016/j.gtc.2014.02.004
8. Katzka DA. The complex relationship between eosinophilic esophagitis and gastroesophageal reflux disease. *Dig Dis.* 2014;32:93-7. doi:10.1159/000357080
9. Ludvigsson JF, Lashkariani M. Cohort profile: ESPRESSO (Epidemiology Strengthened by histoPathology Reports in Sweden). *Clin Epidemiol.* 2019;11:101-14. doi:10.2147/CLEP.S191914
10. Jakobsson GL, Sternegard E, Olen O, Myrelid P, Ljung R, Strid H, et al. Validating inflammatory bowel disease (IBD) in the Swedish National Patient Register and the Swedish Quality Register for IBD (SWIBREG). *Scand J Gastroenterol.* 2017;52:216-21. doi:10.1080/00365521.2016.1246605
11. Svensson M, Bergman D, Olen O, Myrelid P, Bohr J, Wickbom A, et al. Validating microscopic colitis (MC) in Swedish pathology registers. *Scand J Gastroenterol.* 2018;53:1469-75. doi:10.1080/00365521.2018.1543446
12. Ludvigsson JF, Haberg SE, Knudsen GP, Lafolie P, Zoega H, Sarkkola C, et al. Ethical aspects of registry-based research in the Nordic countries. *Clin Epidemiol.* 2015;7:491-508. doi:10.2147/CLEP.S90589
13. Collins MH. Histopathology of eosinophilic esophagitis. *Dig Dis.* 2014;32:68-73. doi:10.1159/000357012
14. Blanchard C, Rothenberg ME. Chemotactic factors associated with eosinophilic gastrointestinal diseases. *Immunol Allergy Clin North Am.* 2009;29:141-8, xi. doi:10.1016/j.iac.2008.10.002
15. Ludvigsson JF, Andersson E, Ekbom A, Feychtting M, Kim JL, Reuterwall C, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health.* 2011;11:450. doi:10.1186/1471-2458-11-450
16. Safroneeva E, Coslovsky M, Kuehni CE, Zwahlen M, Haas NA, Panczak R, et al. Eosinophilic oesophagitis: relationship of quality of life with clinical, endoscopic and histological activity. *Aliment Pharmacol Ther.* 2015;42:1000-10. doi:10.1111/apt.13370
17. Straumann A, Aceves SS, Blanchard C, Collins MH, Furuta GT, Hirano I, et al. Pediatric and adult eosinophilic esophagitis: similarities and differences. *Allergy.* 2012;67:477-90. doi:10.1111/j.1365-2222.2012.02787.x

18. Kapel RC, Miller JK, Torres C, Aksoy S, Lash R, Katzka DA. Eosinophilic esophagitis: a prevalent disease in the United States that affects all age groups. *Gastroenterology*. 2008;134:1316-21. doi:10.1053/j.gastro.2008.02.016
19. Veerappan GR, Perry JL, Duncan TJ, Baker TP, Maydonovitch C, Lake JM, et al. Prevalence of eosinophilic esophagitis in an adult population undergoing upper endoscopy: a prospective study. *Clin Gastroenterol Hepatol*. 2009;7:420-6, 6 e1-2. doi:10.1016/j.cgh.2008.10.009
20. Mackenzie SH, Go M, Chadwick B, Thomas K, Fang J, Kuwada S, et al. Eosinophilic oesophagitis in patients presenting with dysphagia--a prospective analysis. *Aliment Pharmacol Ther*. 2008;28:1140-6. doi:10.1111/j.1365-2036.2008.03795.x
21. Hruz P, Straumann A, Bussmann C, Heer P, Simon HU, Zwahlen M, et al. Escalating incidence of eosinophilic esophagitis: a 20-year prospective, population-based study in Olten County, Switzerland. *J Allergy Clin Immunol*. 2011;128:1349-50 e5. doi:10.1016/j.jaci.2011.09.013
22. Prasad GA, Alexander JA, Schleck CD, Zinsmeister AR, Smyrk TC, Elias RM, et al. Epidemiology of eosinophilic esophagitis over three decades in Olmsted County, Minnesota. *Clin Gastroenterol Hepatol*. 2009;7:1055-61. doi:10.1016/j.cgh.2009.06.023
23. Altun R, Akbas E, Yildirim AE, Ocal S, Korkmaz M, Selcuk H. Frequency of eosinophilic esophagitis in patients with esophageal symptoms: a single-center Turkish experience. *Dis Esophagus*. 2013;26:776-81. doi:10.1111/j.1442-2050.2012.01395.x
24. Lucendo AJ, Arias A, Molina-Infante J. Efficacy of Proton Pump Inhibitor Drugs for Inducing Clinical and Histologic Remission in Patients With Symptomatic Esophageal Eosinophilia: A Systematic Review and Meta-Analysis. *Clin Gastroenterol Hepatol*. 2016;14:13-22 e1. doi:10.1016/j.cgh.2015.07.041
25. Leigh LY, Spergel JM. An in-depth characterization of a large cohort of adult patients with eosinophilic esophagitis. *Ann Allergy Asthma Immunol*. 2019;122:65-72 e1. doi:10.1016/j.anai.2018.09.452
26. Internetmedicin. Eosinofil esofagit . 2019-03-06. <https://www.internetmedicin.se/page.aspx?id=6276>.
27. Zhan T, Ali A, Choi JG, Lee M, Leung J, Dellon ES, et al. Model to Determine the Optimal Dietary Elimination Strategy for Treatment of Eosinophilic Esophagitis. *Clin Gastroenterol Hepatol*. 2018;16:1730-7 e2. doi:10.1016/j.cgh.2018.04.013
28. Spergel J, Aceves SS. Allergic components of eosinophilic esophagitis. *J Allergy Clin Immunol*. 2018;142:1-8. doi:10.1016/j.jaci.2018.05.001
29. Vernon N, Shah S, Lehman E, Ghaffari G. Comparison of atopic features between children and adults with eosinophilic esophagitis. *Allergy Asthma Proc*. 2014;35:409-14. doi:10.2500/aap.2014.35.3768
30. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155:1022-33 e10. doi:10.1053/j.gastro.2018.07.009
31. Dellon ES, Erichsen R, Pedersen L, Shaheen NJ, Baron JA, Sorensen HT, et al. Development and validation of a registry-based definition of eosinophilic esophagitis in Denmark. *World J Gastroenterol*. 2013;19:503-10. doi:10.3748/wjg.v19.i4.503
32. Collins MH, Martin LJ, Alexander ES, Boyd JT, Sheridan R, He H, et al. Newly developed and validated eosinophilic esophagitis histology scoring system and evidence that it outperforms peak eosinophil count for disease diagnosis and monitoring. *Dis Esophagus*. 2017;30:1-8. doi:10.1111/dote.12470