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Subcutaneous immunotherapy in patients with eosinophilic esophagitis

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While the association between eosinophilic esophagitis (EoE) and food allergens is well established, a large proportion of EoE patients have concomitant atopic disease and there is growing evidence that aeroallergens may play a role in pathogenesis.^{1–3} However, subcutaneous immunotherapy (SCIT) for treatment of EoE has not been extensively described.^{4–8} The aim of this study was to compare characteristics and treatment outcomes in patients with EoE who were treated with SCIT (EoE+SCIT) to those who were not treated with SCIT (EoE-SCIT).

We conducted a retrospective cohort study using the University of North Carolina (UNC) EoE clinicopathologic database,⁹ focusing on patients of all ages from 2008 (the year that International Classification of Disease, version-9 [ICD-9] released an EoE code)¹⁰ through 2016. To be included, patients met consensus guidelines for an incident diagnosis of EoE as published at the time of this study design.¹ This study was approved by the UNC Institutional Review Board.

To capture all EoE patients as well as all patients treated with SCIT, we queried the Carolina Data Warehouse for Health, a central data repository containing granular patient information with searchable fields derived from the UNC electronic medical record. We used ICD-9/10 codes, as well as Current Procedure Terminology (CPT) codes for the search. EoE was identified with 530.13 and K20.0. SCIT treatments were identified with CPT codes 95115,

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95117, 95120, 95125, and 95165. We cross-referenced confirmed EoE patients and those treated with SCIT to identify EoE+SCIT and EoE-SCIT subjects, and extracted relevant data from the medical record (Supplemental Methods).

SCIT was based on percutaneous testing or ImmunoCAP allergen-specific IgE measurement. All allergen extracts from Greer Laboratories (Lenoir, NC). Histologic response to treatment was defined as a peak esophageal eosinophil count <15 eos/hpf.^{1,9} Symptom response was defined as the clinically reported patient global response (yes/no). We compared clinical, endoscopic, and histologic characteristics between EoE+SCIT and EoE-SCIT (Supplemental Methods).

Of 692 patients identified with EoE, 25 (3.6%) had CPT codes for SCIT. Of those 25, 15 did not meet inclusion (Supplemental Figure 1). When comparing the EoE-SCIT (n=667) and EoE+SCIT (n=10) groups, age, sex, race, and baseline endoscopic and histologic features were similar (Table 1). The symptom duration prior to diagnosis of EoE was shorter in EoE-SCIT as compared to EoE+SCIT cohort (7.3 vs. 13.8 years; p=0.046). As expected, the EoE+SCIT group had a higher rate of atopic disease.

For EoE+SCIT patients, immunotherapy dose remained consistent throughout the treatment course. The SCIT administered included dust mites, cat, dog, cockroach, tree, grass, weed, ragweed, English plantain, and Alternaria (Supplemental Table 1). Of the 10 cases, 9 were diagnosed with EoE before the administration of SCIT and none of the patients had started SCIT by the time of their first follow-up endoscopy after diagnosis, so we were able to assess initial treatment response in the absence of SCIT. Median follow-up time was 400 days.

After initial diagnosis, these 10 patients were treated with a topical steroid. At the first follow-up endoscopy, 3 (30%) had histological response and 6 (60%) had a symptom response. Of the 5 patients who had follow-up data and were concurrently treated with SCIT, 40% had a histological response and 40% had a symptom response. This did not vary by season of follow-up. These 5 patients had 20% histological response and 40% symptomatic response after initial treatment prior to SCIT. Compared to the initial EGD, at follow up in the EoE+SCIT group there was less use of topical steroids (80% vs. 40%) and more use of dietary elimination (0% vs. 80%) (Supplemental Table 2). There were no adverse outcomes identified in the EoE+SCIT cohort.

The data from this study merit discussion. There were few differences between the EoE+SCIT vs EoE-SCIT groups, and due to a small number of patients treated with SCIT, we are unable to make firm conclusions regarding the impact on treatment outcomes. However, in this selected population there was no decrement in histologic response rates or worsening of global symptom responses in the EoE+SCIT cohort.

There is little literature exploring safety and efficacy of SCIT for EoE treatment.⁴⁻⁸ Ramirez et al describe a 4-year-old boy with refractory EoE who responded histologically and symptomatically to SCIT to dust mites.⁵ De Swert et al describe a 10-year-old boy who had symptomatic and histologic improvement after desensitization with SCIT to grass and birch allergens.⁴ Castilano et al describe a 30-year-old male who had resolution of symptoms and

normalization of esophageal biopsies after SCIT to dust mites, cockroaches, weeds and trees.⁷ Notably, there is one case reporting exacerbation of symptoms after SCIT to grass pollen, implicating a potential risk in treatment of EoE with SCIT.⁸

Despite our review of a large database of EoE patients and a large data warehouse, we could identify only a small fraction of EoE patients who underwent treatment with SCIT at our center, with even fewer receiving SCIT after the initial diagnosis of EoE. Consequently, we are unable to make definitive conclusions regarding the role of SCIT. The number of cases were limited by a single center study, patients could have been seen by an outside allergy practice to receive SCIT, and some had changes in concomitant EoE treatment that could impact response. Further investigation should include multiple medical centers and community-based practices, as well as limit other treatment changes. Nevertheless, because we only included EoE subjects who we could confirm received SCIT, our data are valid in this small group, and should form the basis for future prospective studies using validated EoE outcomes and standardized SCIT protocols.

In conclusion, with the exception of increased atopic disease and longer duration of symptoms, there were few differences between EoE+SCIT and EoE-SCIT patients. The EoE +SCIT group had relatively low initial treatment response rates prior to SCIT. At follow-up, response rates were slightly improved, but in the context of less topical steroids and more dietary elimination. We did not observe any worse outcomes among patients in the EoE +SCIT cohort, suggesting that SCIT in EoE patients may be safe and is worthy of future study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Potential competing interests: Dr. Dellon is a consultant for Adare, Alivio, Allakos, Banner, Calypso, Enumeral, EsoCap, GSK, Gossamer Bio, Receptos/Celgene, Regeneron, Robarts, and Shire, receives research funding from Allakos, Adare, GSK, Meritage, Miraca, Nutricia, Receptos/Celgene, Regeneron, and Shire, and has received an educational grant from Allakos, Banner, and Holoclara. None of the other authors report and potential conflicts of interest with this study.

Abbreviations:

EoE	eosinophilic esophagitis
SCIT	subcutaneous immunotherapy
OIT	oral immunotherapy
EoE-SCIT	eosinophilic esophagitis without subcutaneous immunotherapy
EoE+SCIT	eosinophilic esophagitis with subcutaneous immunotherapy

ICD	international classification of diseases
UNC	University of North Carolina

References

1. Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras C, Katzka DA. ACG Clinical Guideline: Evidence based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis. *Am J Gastroenterol*. 2013;108(5):679–692. [PubMed: 23567357]
2. Pesek RD, Rettiganti M, O'Brien E, et al. Effects of allergen sensitization on response to therapy in children with eosinophilic esophagitis. *Ann Allergy Asthma Immunol*. 8 2017;119(2): 177–183. [PubMed: 28676207]
3. Wolf WA, Jerath MR, Dellon ES. De-novo onset of eosinophilic esophagitis after large volume allergen exposures. *J Gastrointest Liver Dis*. 6 2013;22(2):205–208. [PubMed: 23799220]
4. De Swert L, Veereman G, Bublin M, et al. Eosinophilic gastrointestinal disease suggestive of pathogenesis-related class 10 (PR-10) protein allergy resolved after immunotherapy. *J Allergy Clin Immunol*. 2 2013;131(2):600–602 e601–603. [PubMed: 23374273]
5. Ramirez RM, Jacobs RL. Eosinophilic esophagitis treated with immunotherapy to dust mites. *J Allergy Clin Immunol*. 6 10 2013;132(2):503–504. [PubMed: 23763975]
6. Calderon MA. Could allergen immunotherapy be a therapeutic intervention in eosinophilic oesophagitis? *J Allergy Clin Immunol*. 2016;137 (Suppl 2):AB98.
7. Castilano A, Zacharias D. Immunotherapy as treatment for aeroallergen triggered eosinophilic esophagitis. *Ann Allergy Asthma Immunol*. 2013;111(5):A62.
8. Wells R, Fox AT, Furman M. Recurrence of eosinophilic oesophagitis with subcutaneous grass pollen immunotherapy. *BMJ Case Rep*. 3 15 2018;2018.
9. Runge TM, Eluri S, Woosley JT, Shaheen NJ, Dellon ES. Control of inflammation decreases the need for subsequent esophageal dilation in patients with eosinophilic esophagitis. *Dis Esoph*. 2017;30:1–7.
10. Rybnicek DA, Hathorn KE, Pfaff ER, Bulsiewicz WJ, Shaheen NJ, Dellon ES. Administrative coding is specific, but not sensitive, for identifying eosinophilic esophagitis.. *Dis Esoph*. 2014;27:703–708.

Table 1.

Demographics and clinical characteristics of EoE patients with and without subcutaneous immunotherapy

	EoE-SCIT (n = 667)	EoE+SCIT (n = 10)	P value
Age (mean years $\pm$ SD)	26.0 $\pm$ 18.4	29.2 $\pm$ 14.2	0.59
Male (n, %)	459 (69)	5 (50)	0.20
White (n, %)	532 (81)	9 (90)	0.46
Symptoms (n, %)			
Dysphagia	466 (71)	8 (80)	0.52
Heartburn	249 (39)	4 (40)	0.94
Abdominal pain	143 (22)	1 (10)	0.36
Symptom length prior to diagnosis (mean years $\pm$ SD)	7.3 $\pm$ 8.6	13.8 $\pm$ 8.8	0.046
Atopy (n, %)			
Rhinitis/sinusitis	253 (40)	10 (100)	0.01
Asthma	156 (24)	6 (60)	0.01
Food allergy	173 (29)	4 (44)	0.32
Baseline EGD findings			
Rings	298 (45)	4 (40)	0.75
Stricture	134 (20)	3 (30)	0.45
Narrowing	93 (14)	2 (20)	0.60
Furrows	376 (57)	5 (50)	0.67
Exudates/white plaques	225 (34)	7 (70)	0.02
Edema/decreased vascularity	199 (30)	4 (40)	0.50
Dilation performed	140 (21)	3 (30)	0.50
Baseline eosinophil counts (mean eos/hpf $\pm$ SD)	65.2 $\pm$ 44.7	72.8 $\pm$ 36.5	0.62