

Allergy accelerates the disease progression of chronic rhinosinusitis

Keng-Chung Shen, Yi-Tsen Lin, Chih-Feng Lin, Chin-Hao Chang & Te-Huei Yeh

To cite this article: Keng-Chung Shen, Yi-Tsen Lin, Chih-Feng Lin, Chin-Hao Chang & Te-Huei Yeh (2019): Allergy accelerates the disease progression of chronic rhinosinusitis, Acta Oto-Laryngologica, DOI: [10.1080/00016489.2018.1552368](https://doi.org/10.1080/00016489.2018.1552368)

To link to this article: <https://doi.org/10.1080/00016489.2018.1552368>



Published online: 02 Feb 2019.



Submit your article to this journal [↗](#)



Article views: 5



View Crossmark data [↗](#)

RESEARCH ARTICLE



Allergy accelerates the disease progression of chronic rhinosinusitis

Keng-Chung Shen^{a*}, Yi-Tsen Lin^{a,b*}, Chih-Feng Lin^a, Chin-Hao Chang^c and Te-Huei Yeh^a

^aDepartment of Otolaryngology, College of Medicine, National Taiwan University Hospital, Taipei, Taiwan; ^bGraduate School of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan; ^cDepartment of Medical Research, National Taiwan University Hospital, Taipei, Taiwan

ABSTRACT

Background: The role of allergy in the development of chronic rhinosinusitis (CRS) in East Asians is not clear.

Aims/objectives: The aim was to investigate the impact of allergies in the clinical characteristics of chronic rhinosinusitis.

Material and methods: A total of 138 CRS patients who underwent endoscopic sinus surgery were included. A brief history of rhinosinusitis symptoms, blood eosinophil count, blood-specific allergen tests, computed tomography (CT) scan findings, Lund-Mackay (LM) CT scores, and Sino-Nasal Outcome Test (SNOT-22) Questionnaire scores, and sinuscopy findings at 3 and 6 months postoperatively.

Results: The ImmunoCAP test was positive in 71(51%) patients and negative in 67(49%) patients. The mean age of those who received endoscopic sinus surgery was 7-years younger in the allergic group compared with the non-allergic group ($p = .008$). The peripheral eosinophil count in the allergic group was higher than that of the non-allergic group ($p = .008$). The LM scores and SNOT-22 scores were not significantly different between the two groups. The recurrence rate of nasal polyps in the allergic group was higher but without statistical significance.

Conclusions and significance: Allergy may accelerate the disease progression of CRS. The presence of the serum-specific IgE was correlated with peripheral eosinophil percentage, especially in the CRSwNP patients.

ARTICLE HISTORY

Received 6 October 2018

Revised 6 November 2018

Accepted 18 November 2018

KEYWORDS

Allergy; chronic rhinosinusitis; eosinophil; SNOT-22; Lund-Mackay score

Introduction

Chronic rhinosinusitis (CRS) is a complex multi-factorial inflammatory disease that affects 13.4% of the American [1] and 10.9% of the European [2] general population. The clinical dichotomization of Caucasian patients of CRS with nasal polyps (CRSwNP) versus CRS without nasal polyps (CRSSNP) was reflected at the molecular level, with a predominance of type 1 T helper cells in CRSSNP and of Type 2 T helper cells and eosinophils in patients with CRSwNP [3]. Nevertheless, this definition has proved difficult to be applied to populations in East Asia (i.e. China, Japan, and Korea), because more than half of the CRSwNP patients do not exhibit eosinophil-dominant inflammation [4–6].

The major aeroallergens of our patients are distinct as well. House dust mites (HDM) are the most common allergens and were implicated in 87.8% of our allergic patients, particularly those under 10 years of age [7]. HDM has been reported to disrupt the sinonasal epithelial cell barrier integrity and especially the epithelial tight junction [8]. Allergic rhinitis occurs frequently in patients with CRS. Its prevalence varies from 32% to 84% [9]. Vice versa, the prevalence of CRS is also high in the population with allergies [10]. Therefore, allergies might be important for predisposing or possibly exacerbating the disorder [11,12].

The relationship between allergies and CRS was not clear. Moreover, the severity of CRS in patients with allergies in previous studies was mostly based on computed tomography (CT) scan only [9,10,13]. In this study, we aim to investigate the role of allergies in the clinical characteristics and correlate the severity of CRS by analyzing both subjective symptom and objective CT scan scores.

Materials and methods

Ethical considerations

This retrospective study was conducted at a referral center hospital. Adult patients who were diagnosed with CRS and were undergoing endoscopic sinus surgery as part of the management for their disease were recruited. It was conducted after approval from the Institutional Review Board of National Taiwan University Hospital. All of the patients provided written informed consent for the study participation.

Patients

The eligible patients were aged older than 20 years, had chronic rhinosinusitis and underwent endoscopic sinus

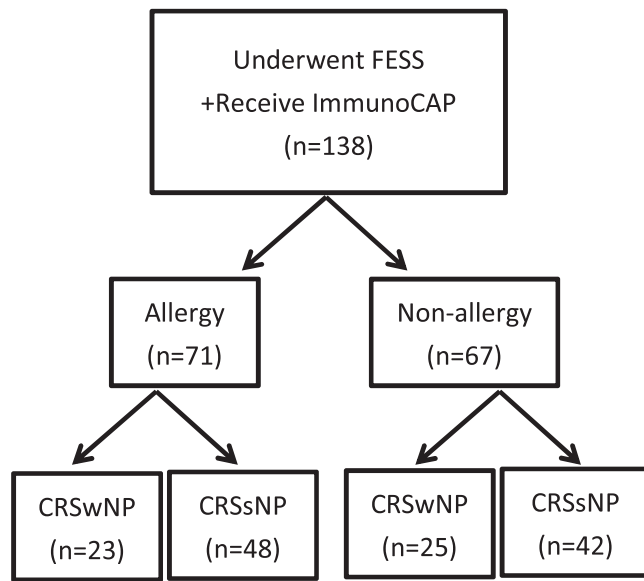


Figure 1. The patient selection flow chart. Among the 138 post-operation CRS patients who had received the ImmunoCAP test, the ImmunoCAP test was positive in 71 (51%) patients (the allergic group) and negative in 67 (49%) patients (the non-allergic group). Among the 71 allergic patients, 23 patients had CRSwNP, and 48 patients had CRSsNP. Among the 67 non-allergic patients 25 patients had CRSwNP, and 42 patients had CRSsNP.

Table 1. Comparisons between the demographics and clinical characteristics of the allergic group and non-allergic group.

Characteristics	Allergy (n = 71)	Non-allergy (n = 67)	p value
Patient characteristics			
Age, years			
In total	42.8 (15.3)	49.8 (15.8)	.008*
Primary ESS only ^a	42.5 (15.1)	50.2 (15.8)	.004*
Gender (M/F)	54/17	37/30	.010*
CRSsNP	48	42	.544
CRSwNP	23	25	.544
SNOT-22 Total score	35.4 (19.1)	41.2 (20.3)	.082
Eosinophil	4.6 (3.5)	3.8 (3.0)	.008*
CRSwNP	5.0 (2.8)	3.3 (2.5)	.031*
CRSsNP	4.3 (3.8)	4.1 (3.4)	.089
Lund-Mackay Score, mean (SD)			
Ostiomeatal complex	2.9 (1.3)	2.6 (1.7)	.426
Anterior ethmoid sinus	2.1 (1.2)	2.3 (1.3)	.215
Maxillary sinus	2.0 (0.9)	2.1 (1.0)	.280
Frontal sinus	1.5 (1.4)	2.0 (1.4)	.029*
Posterior ethmoid sinus	1.7 (1.2)	1.8 (1.3)	.865
Sphenoid sinus	1.0 (1.3)	1.1 (1.3)	.706
Total score	11.2 (5.5)	11.9 (5.9)	.449
Allergic profiles			
Asthma	9	4	.178
Atopic dermatitis	3	1	.339
Allergy to NSAID	2	0	.170
Allergy to penicillin	1	0	.333
Allergy to aspirin	3	0	.091

* $p < .05$.

^aPrimary ESS only: Allergy (n = 70), Non-allergy (n = 64).

surgery between April 2016 and April 2017. The diagnosis of sinus disease was based on the patient's history, clinical examination, nasal endoscopy, and CT scanning of the sinuses according to the European Position Paper on Rhinosinusitis and Nasal Polyps [11]. These patients had previously failed conservative medical therapy for at least 12 weeks. Exclusion criteria were as follows: (1) received oral corticosteroids, monoclonal antibodies, or

Table 2. Comparisons between the individual SNOT22 scores of the atopic group and non-atopic group.

	Allergy Mean (SD)	Non-allergy Mean (SD)	p value
Need to blow nose	2.1(1.5)	2.7(1.6)	.051
Sneezing	1.6(1.4)	1.5(1.4)	.542
Runny nose	1.9(1.5)	2.3(1.5)	.147
Nasal blockage	2.9(1.6)	3.3(1.5)	.179
Decreased sense of smell/taste	2.2(1.8)	2.4(1.9)	.585
Cough	1.4(1.4)	1.8(1.4)	.043*
Post-nasal dripping	2.8(1.4)	3.1(1.4)	.178
Thick nasal discharge	2.2(1.6)	2.9(1.7)	.012*
Ear fullness	0.9(1.2)	1.4(1.4)	.016*
Dizziness	1.3(1.4)	1.6(1.6)	.495
Ear pain	0.4(0.9)	0.8(1.2)	.039*
Facial pain/pressure	0.8(1.2)	0.8(1.1)	.876
Difficulty falling asleep	1.4(1.6)	2.0(1.8)	.089
wake up at night	1.5(1.5)	1.9(1.7)	.140
Lack of a good night's sleep	1.6(1.6)	2.0(1.8)	.318
wake up tired	2.2(1.4)	2.2(1.6)	.867
Fatigue	2.0(1.4)	2.3(1.5)	.462
Reduced productivity	1.4(1.5)	1.6(1.6)	.404
Reduced concentration	1.6(1.5)	1.8(1.5)	.325
Frustrated/restless/irritable	1.3(1.4)	1.5(1.5)	.361
Sad	0.8(1.2)	0.9(1.4)	.927
Embarrassed	0.8(1.2)	0.9(1.4)	.847
SNOT22 total scores	35.4(19.1)	41.2(20.3)	.082

* $p < .05$.

immunosuppressive treatment, during the 1 month period before surgery or (2) established immunodeficiency, coagulation disorder, pregnancy.

Clinical parameters

Pre-operatively, a brief history of rhinosinusitis symptoms and previous treatment, asthma or atopic dermatitis history, past surgical history and history of allergies to aspirin/NSAID/penicillin were recorded. A blood-specific allergen test was performed by the ImmunoCAP test, which is specific for IgE. We also collected the peripheral blood eosinophil count, bacterial culture of nasal discharge, intraoperative endoscopic findings, and CT scan findings before the operation. The sinonasal symptoms were evaluated by the Sino-Nasal Outcome Test (SNOT-22) Questionnaire before the operation. The Lund-Mackay (LM) CT scores were rated by two otolaryngologists independently. We recorded the sinoscopic findings post-operatively at 3 and 6 months to evaluate the recurrence rate.

Statistical analysis

The statistical analysis was performed using SPSS 11.0 (SPSS, Inc., Chicago, IL). When comparisons were made between the groups, the Kruskal–Wallis test was used to establish significant intergroup variability. The Mann–Whitney *U*-test was then used for between-group comparisons. The baseline variables were analyzed using a one-way ANOVA test or Fisher's exact test. Linear regression was used to establish the predictive models, and the main effects of allergies and eosinophilic inflammation on the clinical features of CRS were explored. The significance level was set at a value of 0.05.

Table 3. Comparisons between the clinical characteristics of the patients in the allergic group for the different allergens.

	Derp	Cockroach	SEB	Fungus	Animal	<i>p</i> value	Statistic
Age	40.3 (15.6)	41.5 (17.6)	46.8 (16.7)	45.3 (19.6)	33.3 (10.2)	.308	ANOVA
Number	64	26	20	12	7		
Gender (M/F)	49/15	20/6	15/5	8/4	6/1		
CRSsNP	42	16	14	5	5	.536	ANOVA
CRSwNP	22	10	6	7	2	.536	ANOVA
SNOT22	33.6 (19.1)	28.1 (19.5)	38.9 (15.9)	33.5 (22.2)	45.4 (30.7)	.213	ANOVA
Lund-Mackay Score	11.3 (6.3)	12.2 (5.4)	11.5 (5.1)	12.8 (6.3)	13.3 (3.3)	.837	ANOVA
Asthma	6	1	4	1	0	.403	ANOVA
Eosinophil	5.3 (4.1)	5.5 (4.2)	3.9 (2.3)	4.5 (2.6)	7.1 (6.3)	.359	ANOVA

Table 4. Multivariate linear regression analysis on SNOT-22 & Lund-Mackay score in chronic rhinosinusitis.

	SNOT-22 score		Lund-Mackay score	
	<i>p</i> value	95% C.I.	<i>p</i> value	95% C.I.
Positive serum specific IgE	.0758	−5.9 (−12.5,0.6)	.3873	−0.8 (−2.6,1.0)
Asthma	.0987	9.4 (−1.8,20.6)	.5223	1.0 (−2.1,4.1)
CRSwNP	.0034*	10.2 (3.4,16.9)	<.0001*	4.8 (2.9,6.7)
Peripheral eosinophil	.1727	0.7 (−0.3,1.7)	.1301	0.2 (−0.1,0.5)

p* < .05.Table 5.** Comparisons between the recurrence rates of the CRSwNP patients in the allergic group and non-allergic group.

	Allergy (<i>n</i> = 23)	Non-allergy (<i>n</i> = 25)	<i>p</i> value
Three-months post-operation	4 (17.4%)	2 (8%)	.326
Six-months post-operation	5 (21.7%)	2 (8%)	.178

**p* < .05.

Results

Patient demographics, SNOT-22, and LM scores

In this study, 138 post-operation CRS patients were included. They all had received the ImmunoCAP test (Figure 1). We compared the clinical characteristics between the allergic group and non-allergic group (Table 1). The mean (SD) age of those who received endoscopic sinus surgery was younger in allergic group compared with the non-allergic group (42.8 ± 15.3 years versus 49.8 ± 15.8 years; $p = .008$). The peripheral eosinophil percentage in the allergic group was higher than that of the non-allergic group ($4.6 \pm 3.5\%$ versus $3.8 \pm 3.0\%$; $p = .008$). However, comparing the disease severity and symptoms of CRS, the mean LM score and mean SNOT-22 score showed no significant differences. The distribution of highest LM score located at ostiomeatal complex and subsequently maxillary sinus, anterior ethmoid sinus, posterior ethmoid sinus, frontal sinus, and sphenoid sinus. Only frontal sinus score was significantly different between groups. The presences of CRSwNP, CRSsNP, asthma, atopic dermatitis, NSAID allergy, or aspirin allergy were not different.

For the pre-operative SNOT-22 scores, there were some symptom scores that were significantly higher in the non-allergic group than in the allergic group, which included cough ($p = .043$), thick nasal discharge ($p = .012$), ear fullness ($p = .016$) and ear pain ($p = .039$) (Table 2). In both the allergic and non-allergic groups, nasal blockage had the highest score, which was followed by post-nasal discharge and thick nasal discharge.

Comparisons of the clinical characteristics among the patients with distinct allergens

Among the allergic patients, 64 patients (90%) had allergies to house dust mites, 26 patients (37%) had allergies to cockroaches, 20 patients (28%) had allergies to staphylococcal enterotoxin, 12 patients (17%) had allergies to fungus, and 7 patients (10%) had allergies to animals, but none of the patients had allergies to grass/pollen. The SNOT-22 and LM scores showed no differences among the patients when stratified into the different allergen groups (Table 3).

Multivariate analysis of SNOT-22 and LM scores

In the multivariate analysis, the SNOT-22 subjective symptom scores were significantly greater in the CRSwNP patients (95% CI: 3.4–16.9; $p = .003$). In the multivariate analysis of the LM scores, we observed the same result. The LM score was significantly greater in the CRSwNP patients (95% CI: 2.9–6.7; $p < .001$) (Table 4).

The recurrence of nasal polyps

We followed the CRSwNP patients at 3 and 6 months post-operatively with an endoscopic exam. No matter whether it was 3 months or 6 months postoperation, the recurrence rate in the allergic group was higher than that of the non-allergic group, but this difference did not reach statistical significance (Table 5).

Discussion

Key findings and comparisons with other studies

In this study, the most prominent finding is the mean age of those who received endoscopic sinus surgery was 7-years younger in allergic group compared with the non-allergic group. The peripheral eosinophil count in the allergic group was also significantly higher than that of the non-allergic group. Nevertheless, the LM score and SNOT-22 score were not significantly different between both groups. In the multivariate analysis, CRSwNP was positively correlated with higher SNOT-22 and LM score. Reasonably, the recurrence rate of CRSwNP in the allergic group was higher than that of the non-allergic group but had no significant difference at 3 and 6 months postoperation.

All these evidence indicated that allergy is an accelerating factor of the disease progression resulting in earlier urge for

surgical intervention. Allergies and CRS inflammation may coexist and have a close relationship. Mechanistically, allergic inflammation of the nose changes the integrity of the nasal mucosa and damages the nasal ciliary function. Stasis of nasal secretion may block ostia drainage from the sinus and cause sinus infection [14]. The major allergen in our study was HDM. It has been reported that perennial allergies, especially HDM over seasonal allergens, may potentially contribute to the development of rhinosinusitis [9]. Different from other aeroallergens, exposure to the HDM allergen not only induces the immune reactions of epithelial cells but also impairs the mucosal integrity of the epithelial lining [8]. In our study, the mean age at the time of surgery in the allergic group was significantly younger than that of the non-allergic group. It implies that allergies in CRS patients have detrimental influence of the nasal mucosa because of allergic inflammation and accelerate the disease progression.

Other than CT scores as previous studies, we have examined subjective symptoms scores by the SNOT-22 questionnaire. The same as our result, Abdalla S. et al. found that the most prevalent SNOT-22 scores in patients undergoing surgery for CRS were nasal blockage [15]. In accordance with our study, Robinson et al. found that the symptom scores of CRS patients were not affected by allergic status [16]. Possibly, for the patients who were allergic to perennial allergens, long-term nasal symptoms since childhood may have underscored the SNOT-22 questionnaire preoperatively.

The sinonasal anatomic characteristic is one of the important factors predisposed to CRS. In our study, the observation that highest LM score located at the ostiomeatal complex and subsequently maxillary sinus, anterior ethmoid sinus, posterior ethmoid sinus, frontal sinus, and sphenoid sinus, indicated CRS is a disease centering from the ostiomeatal complex and spreading radially outward. Different weight of contributing factors such as sinonasal anatomic structure and inflammatory load may lead to different direction of disease progression. This was also demonstrated in our recent publication showing that the depth of inflammatory load as a 3-dimensional parameter was needed to evaluate the severity of the refractory CRS [17].

From the literature review, patients with polyps had worse preoperative CT scores than the patients without polyps. The LM score was greater in the CRSwNP patients and asthma patients in the multivariate analysis [13], and eosinophilic CRS had a higher tendency for recurrence after endoscopic sinus surgery than did non-eosinophilic CRS [18]. Accordingly, in our study, CRSwNP was the only factor positively correlated with higher SNOT-22 score and LM score, and the allergic group had a higher recurrence rate in the CRSwNP patients.

Strengths of study

We know that the immune types of chronic rhinosinusitis are different for Caucasians and East Asians. Additionally, the major aeroallergens of our patients are different. In our study, we clarified the relationship between allergies, mainly house dust mite allergies, and chronic rhinosinusitis in our

patient group. By SNOT-22 and LM CT scores, we were able to evaluate the clinical characters of CRS both subjectively and objectively.

Clinical applicability of the study

We have observed that allergy accelerated the disease progression of CRS and the presence of the serum-specific IgE was correlated with peripheral eosinophil percentage, especially in the CRSwNP patients. Systemic allergies may contribute to the formation of nasal polyps with eosinophilic inflammation. To this point, certain intervention for the allergic patient such as environmental modifications may alleviate the development of chronic rhinosinusitis.

Limitations

This cross-sectional observational study has some limitations. Firstly, the ImmunoCAP testing specific for IgE is only 86% as effective in detecting allergies as intradermal testing [19]. The number of allergy patients might be underestimated. Secondly, in this study, the patients were recruited at the time to have a surgical intervention for CRS. Thus, the severity and the symptom scores may reach similar range at the moment to receive sinus surgery. This may render no significant differences in the SNOT-22 and Lund-Mackay scores being observed between the allergic and non-allergic groups. Therefore, further cohort studies should be conducted to avoid this selection bias.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This study was financially supported by the Ministry of Science and Technology [MOST 105-2314-B-002-165].

References

- [1] Pleis JR, Barnes PM. A comparison of respiratory conditions between multiple race adults and their single race counterparts: an analysis based on American Indian/Alaska Native and white adults. *Ethn Health*. 2008;13:399–415.
- [2] Hastan D, Fokkens WJ, Bachert C, et al. Chronic rhinosinusitis in Europe—an underestimated disease: A GA²LEN study. *Allergy*. 2011;66:1216–1223.
- [3] Van Bruaene N, Perez-Novoa CA, Basinski TM, et al. T-cell regulation in chronic paranasal sinus disease. *J Allergy Clin Immunol*. 2008;121:1435–1441; 1441.e1431–1433.
- [4] Zhang N, Van Zele T, Perez-Novoa C, et al. Different types of T-effector cells orchestrate mucosal inflammation in chronic sinus disease. *J Allergy Clin Immunol*. 2008;122:961–968.
- [5] Ishitoya J, Sakuma Y, Tsukuda M. Eosinophilic chronic rhinosinusitis in Japan. *Allergol Int*. 2010;59:239–245.
- [6] Kim JW, Hong SL, Kim YK, et al. Histological and immunological features of non-eosinophilic nasal polyps. *Otolaryngol Head Neck Surg*. 2007;137:925–930.
- [7] Yin SC, Liao EC, Chiu CL, et al. Der p2 internalization by epithelium synergistically augments toll-like receptor-mediated

- proinflammatory signaling. *Allergy Asthma Immunol Res.* 2015;7:393–403.
- [8] Steelant B, Farre R, Wawrzyniak P, et al. Impaired barrier function in patients with house dust mite-induced allergic rhinitis is accompanied by decreased occludin and zonula occludens-1 expression. *J Allergy Clin Immunol.* 2016;137:1043–1053.e5.
- [9] Berrettini S, Carabelli A, Sellari-Franceschini S, et al. Perennial allergic rhinitis and chronic sinusitis: correlation with rhinologic risk factors. *Allergy.* 1999;54:242–248.
- [10] Sedaghat AR, Gray ST, Wilke CO, et al. Risk factors for development of chronic rhinosinusitis in patients with allergic rhinitis. *Int Forum Allergy Rhinol.* 2012;2:370–375.
- [11] Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhin.* 2012;50:1–12.
- [12] Kennedy JL, Borish L. Chronic sinusitis pathophysiology: the role of allergy. *Am J Rhinol Allergy.* 2013;27:367–371.
- [13] Pearlman AN, Chandra RK, Chang D, et al. Relationships between severity of chronic rhinosinusitis and nasal polyposis, asthma, and atopy. *Am J Rhinol Allergy.* 2009;23:145–148.
- [14] Mabry RL. Allergic and infective rhinosinusitis: differential diagnosis and interrelationship. *Otolaryngol Head Neck Surg.* 1994;111:335–339.
- [15] Abdalla S, Alreefy H, Hopkins C. Prevalence of sinonasal outcome test (SNOT-22) symptoms in patients undergoing surgery for chronic rhinosinusitis in the England and Wales National prospective audit. *Clin Otolaryngol.* 2012;37:276–282.
- [16] Robinson S, Douglas R, Wormald PJ. The relationship between atopy and chronic rhinosinusitis. *Am J Rhinol.* 2006;20:625–628.
- [17] Lin KY, Chen PY, Yeh TH. How deep is the inflammation in chronic rhinosinusitis? Sinus wall thickness and blood eosinophilia. *Rhinology.* 2018;56(1):46–53.
- [18] Ikeda K, Shiozawa A, Ono N, et al. Subclassification of chronic rhinosinusitis with nasal polyp based on eosinophil and neutrophil. *Laryngoscope.* 2013;123:E1–E9.
- [19] Kam KL, Hsieh KH. Comparison of three in vitro assays for serum IgE with skin testing in asthmatic children. *Ann Allergy.* 1994;73:329–336.