Type 2 biomarkers and quality of life in chronic rhinosinusitis with nasal polyps

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Type 2 biomarkers and quality of life in chronic rhinosinusitis with nasal polyps

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Historically, chronic rhinosinusitis (CRS) has been categorized as CRS with nasal polyps (CRSwNP) and CRS without nasal polyps.[1] The European Position Paper on Rhinosinusitis and Nasal Polyps 2020 guidelines suggest classifying CRS on the basis of type 2 (T2) biomarkers.[2] Type 2 inflammation is responsible for driving the disease in 80% to 90% of patients with CRSwNP.[1] In clinical practice, peripheral blood eosinophils (PBE) and total IgE may help assess, but cannot fully confirm, whether CRS is driven by T2 inflammation. Peripheral blood eosinophils and IgE reflect T2 cytokines interleukin (IL)-5, and IL-4 and IL-13, respectively. We aimed to assess how PBE and total IgE are associated with symptoms and quality of life using the 22-item sinonasal outcome test (SNOT-22) and objective findings of CRSwNP on the basis of Lund-Mackay score (LMS) on computed tomography imaging and nasal polyp score (NPS) on endoscopy in a real-life otolaryngology secondary care clinic setting.

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This was a retrospective single-center study of patients with CRSwNP with and without asthma, including aspirin-exacerbated respiratory disease (AERD), seen in the clinic during a 24-month period who had completed a SNOT-22 questionnaire and had T2 biomarkers (PBE and total IgE) tested in the previous 6 months. The average values of the T2 biomarkers over the previous 6 months were compared with the reference range (PBE < 300 cells/μL and total IgE < 100 kU/L).[3] The results of PBE and total IgE were excluded when the blood tests were obtained during acute hospital admissions and taken within a 3-month period after receiving oral corticosteroids.

Computed tomography sinus scans performed within 3 months before or after the clinic appointment were included in the analysis, having not had medical polypectomy during that time. The patients who had undergone nasal polyp surgery within the past year or were receiving regular oral corticosteroids (≥5 mg of prednisolone or equivalent daily on a maintenance basis) or biologics were not included.

The patient cohort was divided into the lowest, middle, and highest tertiles for SNOT-22, NPS, and LMS. In addition, we used a previously reported grading of SNOT-22 on the basis of its total score as mild (≤20), moderate (21-50), and severe (>50).[4]

Student's *t* test and Pearson correlation test were used for normally distributed data, and the Mann-Whitney U test, Kruskal-Wallis H test, and Spearman correlation test were used for non-normally distributed data. Statistical significance was determined with a 2-tailed alpha error of 0.05.

A total of 108 patients with CRSwNP were included with a mean age of 53.6 (± 14.2) years. 64.8% are of male sex, 6.5% were current smokers, and 62.9% had asthma (CRSwNP-A), of which 33.8% (21.3% of all the cohort) had AERD (CRSwNP-AERD), whereas 43.5% had previous endoscopic sinus surgery. Both T2 biomarkers were raised in 39.8%, 70.4% had raised PBE, 50.9% had raised total IgE, and 52.3% had one or more positive specific IgE to common aeroallergens. The median NPS (out of 8) was 5 (interquartile range [IQR] 4-6), the mean LMS (out of 24) was 13.2 (± 5.5), and the median SNOT-22 (out of 110) was 43 (IQR 25-61).

Patients with CRSwNP-A had higher counts of T2 biomarkers compared with patients with CRSwNP but without asthma: the median PBE was 430 (IQR 323-658) vs 302 (IQR 200-399) and the median total IgE was 135 (IQR 54-255) vs 61 (IQR 27-111), respectively (both $P < .001$). In addition, CRSwNP-A had a higher mean (95% CI) LMS 14.3 (12.6-16) vs 11.4 (9.7-13.2) ($P = .03$). There were no differences in SNOT-22 scores, number of specific IgE positive to common aeroallergens, and NPS between these 2 groups.

There were significant correlations between SNOT-22 vs PBE and total IgE (r = 0.24, $P = .01$ and r = 0.27, $P = .005$, respectively). The NPS significantly correlated with PBE and total IgE (r = 0.31, $P = .001$, and r = 0.21, $P = 0.03$, respectively), and significantly correlated with LMS (r = 0.45, $P < .001$); however, correlations between LMS and PBE and with total IgE were not significant. These correlations are illustrated in Figure 1.

There was no difference in PBE between patients with mild and severe SNOT-22 scores, although a significant difference in median total IgE was seen between patients with mild and severe SNOT-22 scores (53 [IQR 28-124] vs 146.5 [IQR 146.5-264], $P = .008$).

There was a significant difference in median PBE between patients in the lowest (338, IQR 223-399) and highest (475, IQR 296-647) SNOT-22 tertiles ($P = .046$) and a significant difference in median total IgE between patients in the lowest (64.5, IQR 27.8-127) and highest (155, IQR 61.5-260) SNOT-22 tertiles ($P = .007$). A significant difference in median PBE was between patients in the lowest (318, IQR 235-435) and highest (435, IQR 360-644) NPS tertiles ($P = .01$). No difference in PBE and total IgE was seen between the lowest and highest LMS tertiles.

To put our observations in context, Racette et al[1] reported correlations between SNOT-22 and T2 cytokines including IL-4, IL-5and IL-13 in patients with CRSwNP. However, Chowdhury et al[6] found that mucus IL-4 did not correlate with the total SNOT-22 score whereas Kowalik et al[5] found a correlation between PBE and SNOT-22 in

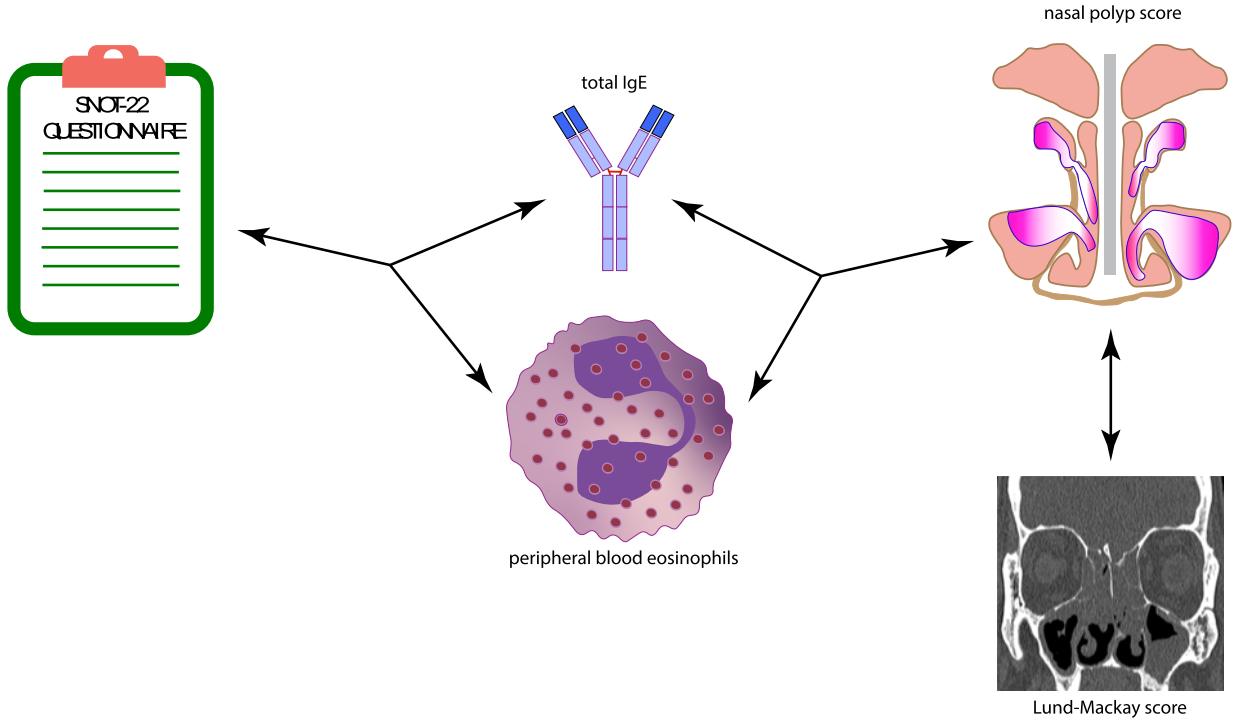

Figure 1. Correlations between subjective and objective measurements of chronic rhinosinusitis with nasal polyps. The arrows represent statistically significant correlations between the assessments and tests.

eosinophilic-CRS (eosinophils >10 per high powered field).[5,6] In our cohort 81.5% of patients with CRSwNP had disease associated with one or both raised T2 biomarkers similar to previous data.[1] Previous reports of CRSwNP with comorbid asthma having higher T2 biomarkers have also been confirmed by our present findings.[7] Interestingly, there were significant differences in T2 biomarkers and LMS but not NPS or SNOT-22 between CRSwNP with vs without asthma. We believe LMS, compared with NPS, reflects better the total underlying mucosal disease burden whereas NPS only reflects the "tip of the iceberg" seen at endoscopy. Hence, we feel that T2 biomarkers follow the same pattern. Nevertheless, the lack of correlation between LMS and the T2 biomarkers is somewhat curious and worthy of further investigation in other cohorts.

Our study has limitations of not having serial measures over time, especially PBE, which may be variable, and data on asthma control for the patients with CRSwNP-A when they presented to the rhinology clinic. We appreciate the impact of asthma control on the quality of life assessed with SNOT-22, therefore, patients with CRSwNP-A should also perform an asthma control questionnaire when SNOT-22 is completed.

In conclusion, our data from an unselected real-life CRSwNP cohort suggest that PBE and total IgE are associated with more severe disease as assessed by either a quality-of-life questionnaire or endoscopy.

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Academic interest of allergists in atopic dermatitis before and after approval of systemic immunomodulators

Atopic dermatitis (AD) is a common inflammatory skin disease that has traditionally been managed by dermatologists. In March 2017, the US Food and Drug Administration (FDA) approved the first biologic, dupilumab, for the treatment of moderate to severe AD.[1] Dupilumab is a monoclonal antibody that targets interleukin (IL)-4 and IL-13, which are the leading causes of allergic inflammation in various conditions including AD, asthma, eosinophilic esophagitis, and chronic rhinosinusitis with nasal polyps. Since the approval of dupilumab, the FDA has approved 3 additional systemic immunomodulators for the treatment of AD.[2] Tralokinumab, a human IgG4 monoclonal antibody that inhibits the bioactivity of IL-13, and abrocitinib and upadacitinib, which are Janus kinase inhibitors, target type 2 immune response and proinflammatory pathways.[3] In this study, we hypothesize that academic interest of allergists in AD has increased since the approval of these systemic immunomodulators. We compared the number of articles on AD that were published in top-ranked allergy and dermatology journals before and after the approval of systemic immunomodulators for AD.

Academic interest based on the number of published papers on AD among allergy and dermatology journals was assessed using the method of Correll and Kissin.[4] Briefly, the analysis was carried out using the PubMed database of the National Library Medicine's website. We used the medical subject heading term of "atopic dermatitis." We also included "atopic dermatitis" under the category of "Other

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