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ORIGINAL RESEARCH

Rheumatoid Arthritis Exacerbates Eosinophilic Inflammation Contributing to Postoperative Recurrence in Chronic Rhinosinusitis with Nasal Polyps

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Objective: To assess the impact of rheumatoid arthritis (RA) on histopathological features and the risk of postoperative recurrence in chronic rhinosinusitis with nasal polyps (CRSwNP) patients.

Methods: A retrospective cohort study of CRSwNP patients who underwent functional endoscopic sinus surgery was performed. Patients were followed up for more than two years, and classified into RA and Non-RA groups, recurrent and non-recurrent groups. The influence of RA on histopathological features and the risk of CRSwNP recurrence was explored.

Results: A total of 517 CRSwNP patients were finally recruited, including 78 RA patients. The RA group exhibited a higher recurrence rate, tissue eosinophil counts and percentages compared to the non-RA group ($P < 0.05$). Tissue eosinophil count and percentage, and the prevalence of allergic rhinitis were significantly higher in the recurrent group in compared to the non-recurrent group ($P < 0.05$). Multivariate logistic regression analysis identified tissue eosinophil count and percentage, RA, and allergic rhinitis as significant predictors of increased recurrence risk ($P < 0.05$). Both adjusted and unadjusted models affirmed RA as an independent risk factor for CRSwNP postoperative recurrence ($P < 0.05$). Kaplan-Meier curves further indicated a higher recurrence risk in CRSwNP patients with RA than those without ($P < 0.05$).

Conclusion: Our findings suggest that RA significantly exacerbates tissue eosinophilic inflammation and independently heightens the risk of postoperative recurrence in CRSwNP patients. These insights underscore the need for tailored therapeutic strategies addressing the complex interplay between CRSwNP and RA to mitigate recurrence risks and improve clinical outcomes.

Keywords: rheumatoid arthritis, chronic rhinosinusitis with nasal polyps, endoscopic sinus surgery, recurrence

Introduction

Chronic rhinosinusitis (CRS) is a common and multifactorial inflammatory disease of the nasal cavity and paranasal sinus mucosa, involving complex interactions between environmental, genetic, and immune factors.[1,2] CRS manifests with typical symptoms such as nasal congestion, purulent nasal discharge, olfactory dysfunction, and headaches.[3–5] CRS can be divided into two phenotypes: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). As a unique CRS phenotype, CRSwNP has more obvious symptoms, a higher postoperative recurrence rate, and significantly impaired olfactory function than CRSsNP, which are clinical features that attract more attention from clinicians.[6–8] Increasing evidence suggests that the histopathological features of CRSwNP are highly heterogeneous, and accompanying diseases further exacerbate the complexity of its pathological mechanisms.[9–11] Recently, functional endoscopic sinus surgery (FESS) has become the favored surgical approach for CRSwNP patients who responded poorly to pharmacological treatments, owing to its effectiveness and safety.[12,13] However, despite advancements in surgical techniques,

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postoperative recurrence remains high and continues to be a significant challenge in managing CRSwNP. This challenge is primarily driven by the unclear etiology of the disease, high tissue heterogeneity, and the complexity introduced by comorbid conditions.[14–16] Several potential risk factors have been identified, including disease duration, eosinophilic inflammation, nasal microbiota dysbiosis, and comorbidities such as allergic rhinitis (AR), hyperuricemia, and metabolic syndrome, all of which have been linked to an increased risk of CRSwNP recurrence.[17–21]

Understanding the additional factors that contribute to postoperative recurrence in CRSwNP is critical for improving patient prognosis and optimizing treatment strategies. Recent studies have increasingly highlighted the connection between CRSwNP and systemic inflammatory conditions, such as rheumatoid arthritis (RA). Furthermore, both conditions are thought to share common immune pathways, involving cytokines and immune cells, which may contribute to similar pathogenic mechanisms.[22] RA is an autoimmune disease characterized by systemic inflammation and extra-articular manifestations, including those affecting the respiratory system.[23] It is well-established that RA can lead to systemic inflammation and immune dysregulation, potentially impacting various organ systems beyond the joints, including complications like pleuritis, valvular heart disease, interstitial lung disease, and nasal and paranasal sinus impairments.[24,25] A recent study reported a higher incidence of CRS in patients with RA, suggesting that RA may contribute to nasal mucosal damage and play a role in the pathogenesis of CRS.[26] Another publication found an increased prevalence of Staphylococcus aureus nasal carriage in rheumatoid arthritis patients, which may contribute to the development of CRS.[27] However, the influence of RA on the clinical and histopathological features of CRSwNP patients remains unexplored, and knowledge about the interrelation between RA and CRSwNP recurrence is sparse. The presence of RA in CRSwNP patients raises concerns about potentially more complicated disease progressions and challenges in managing postoperative outcomes. Identifying the clinical and histopathological characteristics of CRSwNP patients with concurrent RA as a distinct disease subgroup and assessing whether RA contributes to increased tissue heterogeneity and postoperative CRSwNP recurrence are crucial.

This study is designed to rigorously assess the potential association between RA and eosinophilic inflammation, as well as postoperative recurrence, in patients with CRSwNP. Our objective is to analyze the clinical features and outcomes of FESS in CRSwNP patients who also suffer from RA, to deepen our understanding of how these conditions interact. By exploring the relationship between RA and both eosinophilic inflammation and postoperative recurrence in CRSwNP, this research could significantly influence the optimization of treatment approaches and enhance the management of post-operative outcomes for this patient group.

Materials and Methods

Ethical Statement

This retrospective cohort study was approved by the Human Ethical Committee in Xiangya Hospital of Central South University (2021091148). As the study did not involve any private patient information or commercial interests, the Ethics Committee waived the requirement for informed consent. This study complies with the Declaration of Helsinki.

Participants, Study Design, and Data Collection

This study included CRSwNP patients who underwent FESS at our medical center between January 1, 2019, and December 31, 2021. The inclusion criteria of CRSwNP patients were as follows:[1] adherence to the guidelines for diagnosis and treatment of CRSwNP;[28] (2) age between 18 and 70 years old; (3) complete clinical data; (4) no previous history of FESS; (5) no comorbidity with other autoimmune diseases other than RA. The exclusion criteria of CRSwNP patients included the follows: (1) with fungal sinusitis, allergic fungal rhinosinusitis, sinus benign or malignant tumor; (2) with severe systemic organic disease or current acute inflammation; (3) previous radiotherapy history; (4) loss of follow-up; (6) RA in the acute status; (7) received immunomodulatory drugs or biologics treatment within one month before FESS. All patients underwent detailed medical history inquiries and records, nasal endoscopy examinations, laboratory examinations, and sinus computed tomography.

The baseline characteristics and clinical data were obtained from the electronic medical records. The Lund-MacKay score and Lund-Kennedy score were used to assess the severity of CRSwNP patients' preoperative symptoms as

previously described.[11] Preoperative data including age, gender, smoking, alcohol, duration of disease, body mass index (BMI), RA, diabetes mellitus, hypertension, AR, and asthma were collected. In addition, laboratory data, specifically erythrocyte sedimentation rate, hypersensitive C-reactive protein, anti-cyclic citrulline peptide antibody, rheumatoid factor, systolic blood pressure, diastolic blood pressure, and fasting blood glucose, were measured in the hospital biochemistry department. A diagnosis of RA was performed based on the 2010 classification criteria of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR 2010).[23]

Follow-Up and Postoperative Recurrence Definition

All FESS surgical procedures were carried out by the same medical team. A uniform postoperative care protocol was adhered to for all patients, which included daily nasal saline irrigations, antibiotics, topical corticosteroids, and routine endoscopic cleanings. Postoperative evaluations were conducted using nasal endoscopy at one month, three months, six months, and subsequently every six months to one year to monitor patient outcomes. All patients were followed up for more than two years, with the endpoint being either the recurrence of the disease or the end of the follow-up interval. Recurrence was determined by the reappearance of clinical symptoms along with endoscopic and computed tomography findings, persisting for at least two months despite a treatment intervention involving antibiotics and oral steroids as previously outlined.[20,29]

Tissue Eosinophil Quantification

Nasal polyp tissues were obtained during surgery and subsequently preserved in 4% paraformaldehyde. Post-fixation, these samples were embedded in paraffin wax and sectioned into 4 μm slices. The sections were then stained using hematoxylin and eosin (HE). Each stained sample was examined at a high-power field (HPF) magnification of ×400 to evaluate the infiltration of inflammatory cells, with a specific focus on eosinophils. The eosinophil count was calculated by averaging the counts from five HPF chosen at random, and the eosinophil percentage was determined by computing the ratio of eosinophils to the total number of inflammatory cells observed.

Statistical Analysis

Categorical variables were presented as percentages and numbers, and compared utilizing the chi-squared test. Quantitative variables with normal distribution were shown as mean ± standard deviation and compared with the Student's *t*-test between the two groups. Those data without normal distribution were presented as median and interquartile ranges (IQRs), and the Mann–Whitney *U*-test was utilized in the comparison between the two groups. CRSwNP patients were categorized into non-recurrent and recurrent CRSwNP groups, and logistic regression analysis was performed to identify factors that affect the recurrence of CRS postoperatively. Additionally, the association between RA and the risk of CRS recurrence was further analyzed using various adjusted models. Kaplan-Meier survival curves and multivariate regression analysis were performed and explore RA association with the risk of CRSwNP recurrence. Statistical significance was regarded as a two-tailed $P < 0.05$.

Results

Characteristics and Baseline Data of the Study Subjects

In the original cohort, 558 CRSwNP patients were initially included. After exclusion criteria were applied, 41 patients were excluded, leaving 517 patients available for analysis. These subjects were divided based on the presence of RA into two groups: CRSwNP patients with RA (n = 78) and CRSwNP patients without RA (n = 439). Furthermore, based on the outcomes observed during follow-up, patients were also categorized into the recurrent CRSwNP group (n = 117) and the non-recurrent CRSwNP group (n = 400). Figure 1 shows the flowchart of CRSwNP recruitment and grouping.

The baseline characteristics and clinical data between non-RA and RA groups are detailed in Table 1. The mean age of the participants was 45.0 years, and the cohort comprised predominantly males (338 or 65.4%). Among these, 78 patients also had a diagnosis of comorbid RA. The average duration of postoperative follow-up was 31.4 months. By the end of this period, postoperative recurrence had been identified in 117 (22.6%) of the CRSwNP patients. After categorizing the patients based on RA status, we analyzed the postoperative recurrence rates between the RA and non-

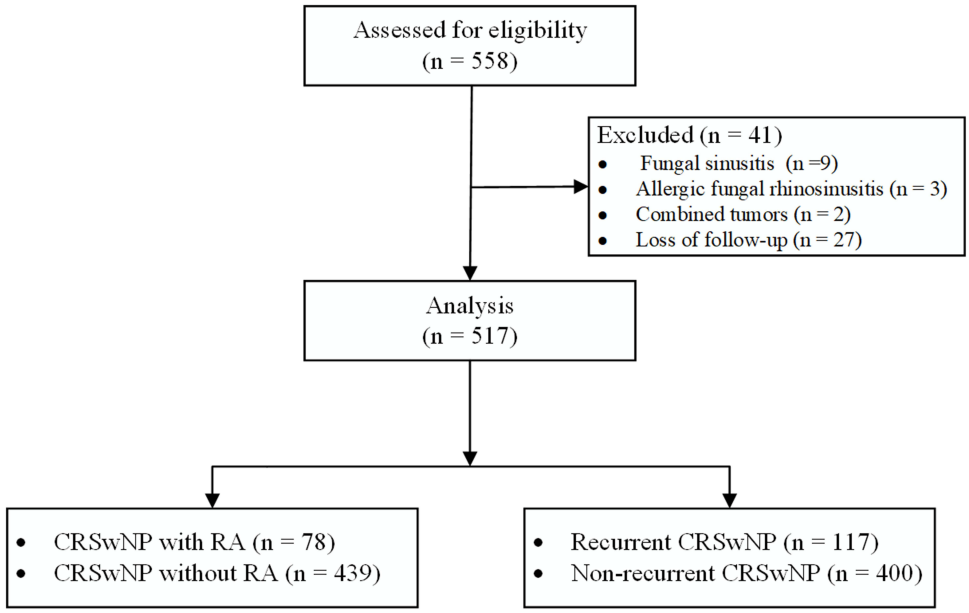

Figure 1 The flowchart of CRSwNP recruitment and grouping.
Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; RA, rheumatoid arthritis.

RA groups. As shown in Table 1, patients with RA exhibited significantly higher rates of postoperative recurrence compared to those without RA ($P < 0.05$). Additionally, the RA group displayed a greater proportion of female patients, a higher prevalence of diabetes mellitus, and significantly elevated values for BMI, Lund-MacKay score, Lund-Kennedy score, and both the count and percentage of tissue eosinophils compared to the non-RA group ($P < 0.05$).

Table 1 Baseline Clinical Characteristics of CRSwNP Patients

Variables	All (n=517)	Non-RA (n=439)	RA (n=78)	P
Age, years	45.0 (32.0–55.0)	45.0 (31.0–55.0)	45.5 (32.0–55.0)	0.569
Male, n (%)	338 (65.4)	312 (71.1)	26 (33.3)	<0.001
Smoking, n (%)	87 (16.8)	70 (16.0)	17 (21.8)	0.203
Alcohol, n (%)	37 (7.2)	28 (6.4)	9 (11.5)	0.103
Duration of disease, months	24.0 (6.0–60.0)	24.0 (6.0–71.0)	13.5 (6.0–48.0)	0.097
BMI, kg/m^2	21.8 (19.7–24.6)	21.5 (19.5–24.0)	24.1 (21.2–25.9)	<0.001
Tissue eosinophil count (n/HPF)	9.5 (4.0, 21.5)	6.5 (4.0, 17.0)	14.0 (7.0, 34.5)	<0.001
Tissue eosinophil percentage (%)	8.4 (4.9, 18.8)	7.6 (4.8, 17.3)	14.7 (6.9, 41.1)	<0.001
Diabetes mellitus, n (%)	87 (16.8)	66 (15.0)	21 (26.9)	0.042
Hypertension, n (%)	92 (17.8)	81 (18.5)	11 (14.1)	0.355
SBP, mmHg	125.0 (115.0–136.0)	125.0 (115.0–136.0)	122.5 (114.0–136.0)	0.831
DBP, mmHg	80.0 (72.5–86.0)	80.0 (72.0–86.0)	80.0 (74.8–87.0)	0.376
Allergic rhinitis, n (%)	112 (21.7)	90 (20.5)	22 (28.2)	0.128
Asthma, n (%)	26 (5.0)	21 (4.8)	5 (6.4)	0.745
Lund-MacKay score	10.5 (9.5, 14.5)	9.5 (8.0, 12.5)	13.0 (10.0, 15.5)	<0.001
Lund-Kennedy score	7.0 (5.5, 9.0)	6.0 (5.0, 7.0)	7.5 (6.5, 11.0)	0.009
ESR (mm/h)			35.8 (28.4, 40.8)	
Hs-CRP (mg/L)			17.3 (9.7, 27.3)	
Anti-CCP (U/mL)			765.3 (431.6, 989.6)	
RF (U/mL)			234.6 (198.5, 301.1)	
Recurrent CRSwNP, n (%)	117 (22.6)	89 (20.3)	28 (35.9)	0.002
Follow-up time, months	31.4 (23.9–45.7)	32.8 (23.6–47.3)	30.2 (21.6–45.5)	0.689

Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; RA, rheumatoid arthritis; BMI, body mass index; HPF, high-power field; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESR, erythrocyte sedimentation rate; hs-CRP, hypersensitive C-reactive protein; Anti-CCP, anti-cyclic citrulline peptide antibody; RF, Rheumatoid factor.

RA and the Risk of Postoperative Recurrence in CRSwNP

To investigate the association between RA and the risk of CRSwNP recurrence, we further categorized study subjects into the non-recurrent CRSwNP group and the recurrent CRSwNP group. As presented in Table 2, The tissue eosinophil count and percentage, and the rate of AR and RA were significantly elevated in the recurrent CRSwNP group compared to the non-recurrent CRSwNP group ($P < 0.05$). However, there was no significant difference in other variables between the two groups ($P > 0.05$).

We conducted a multivariate logistic regression analysis to explore potential risk factors for recurrence of CRSwNP. According to the results presented in Table 3, there was a significant association between higher risks of CRSwNP

Table 2 Baseline Clinical Characteristics Between Non-Recurrent and Recurrent CRSwNP Groups

Variables	Non-recurrent CRSwNP (n=400)	Recurrent CRSwNP (n=117)	P
Age, years	45.0 (31.0–55.0)	45.0 (32.5–55.0)	0.373
Male, n (%)	258 (65.0)	80 (68.4)	0.438
Smoking, n (%)	70 (17.5)	17 (14.5)	0.450
Alcohol, n (%)	31 (7.8)	6 (5.1)	0.333
Duration of disease, months	24.0 (6.0–60.0)	24.0 (6.0–84.0)	0.499
BMI, kg/m^2	21.8 (19.6–24.6)	22.3 (19.9–24.9)	0.616
Tissue eosinophil count (n/HPF)	5.5 (4.5, 12.0)	17.5 (8.5, 38.0)	<0.001
Tissue eosinophil percentage (%)	6.7 (4.8, 14.8)	16.1 (6.9, 42.5)	<0.001
Diabetes mellitus, n (%)	61 (15.3)	26 (22.2)	0.076
Hypertension, n (%)	75 (18.8)	17 (14.5)	0.294
SBP, mmHg	125.0 (115.0–136.0)	125.0 (114.5–134.5)	0.893
DBP, mmHg	80.0 (73.0–87.0)	80.0 (72.0–85.0)	0.620
Allergic rhinitis, n (%)	75 (20.8)	37 (24.8)	0.003
Asthma, n (%)	18 (4.5)	8 (6.8)	0.309
RA, n (%)	50 (12.5)	28 (23.9)	0.002

Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; BMI, body mass index; HPF, high-power field; SBP, systolic blood pressure; DBP, diastolic blood pressure; RA, rheumatoid arthritis.

Table 3 Multivariate Analysis of Risk Factors for CRSwNP Recurrence

Variables	Multivariate		
	OR	95% CI	P
Age	1.010	0.994–1.026	0.213
Gender			
Male	1.592	0.972–2.608	0.065
Female (ref.)			
Smoking			
Yes	0.886	0.456–1.725	0.723
No (ref.)			
Alcohol			
Yes	0.599	0.210–1.714	0.340
No (ref.)			
Duration of disease	1.003	0.992–1.005	0.068
BMI	0.977	0.918–1.040	0.464
Tissue eosinophil count	1.354	1.112–2.238	<0.001
Tissue eosinophil percentage	1.531	1.363–2.771	<0.001

(*Continued*)

Table 3 (Continued).

Variables	Multivariate		
	OR	95% CI	P
Diabetes mellitus			
Yes	0.754	0.351–1.620	0.469
No (ref.)			
Hypertension			
Yes	0.743	0.404–1.366	0.339
No (ref.)			
Allergic rhinitis			
Yes	1.956	1.186–3.224	0.009
No (ref.)			
Asthma			
Yes	1.095	0.424–2.825	0.852
No (ref.)			
RA			
Yes	2.739	1.520–4.936	0.001
No (ref.)			

Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; OR, odds ratio; CI, confidence interval; RA, rheumatoid arthritis.

Table 4 Unadjusted and Adjusted Logistic Regression Analysis for CRSwNP Recurrence According to RA

Variables	OR	95% CI	P
Unadjusted	2.202	1.312–3.696	0.003
Model 1	2.582	1.482–4.500	0.001
Model 2	2.781	1.581–4.889	<0.001
Model 3	2.627	1.437–4.651	0.001

Notes: Model 1: Adjusted for age and gender; Model 2: Adjusted for age, gender, smoking, duration of disease, alcohol, allergic rhinitis, and asthma; Model 3: Adjusted for age, gender, smoking, duration of disease, alcohol, allergic rhinitis, asthma, tissue eosinophil count and percentage.
Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; RA, rheumatoid arthritis; OR, odds rate; CI, confidence interval.

recurrence and factors such as tissue eosinophil count and percentage, RA, and AR ($P < 0.05$). Additionally, RA was evaluated as a standalone variable in both unadjusted and adjusted logistic regression analyses to further assess its impact on CRSwNP recurrence. The findings, displayed in Table 4, indicated that RA significantly elevated the risk of postoperative recurrence ($P < 0.05$), even when adjusting for various potential confounders across different models. Moreover, Kaplan-Meier survival curves, illustrated in Figure 2, showed that the non-RA group had a lower recurrence risk compared to the RA group ($P < 0.05$).

Discussion

To our knowledge, this study is the first to investigate the effects of RA on eosinophilic inflammation in tissue and postoperative recurrence among CRSwNP patients, using a relatively large retrospective cohort. We discovered that RA

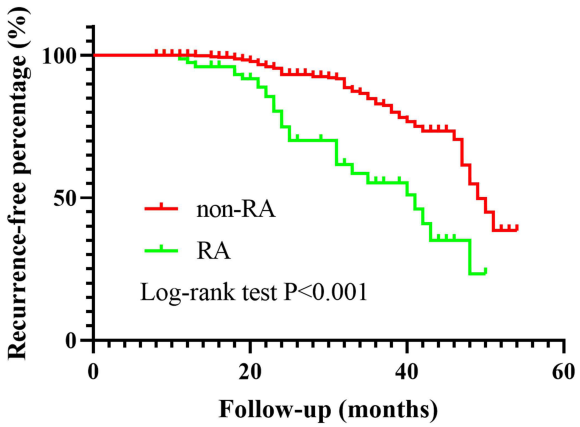

Figure 2 Kaplan–Meier survival curves stratified by RA and non-RA in predicting the postoperative recurrence of CRSwNP.
Abbreviations: RA, rheumatoid arthritis; CRSwNP, chronic rhinosinusitis with nasal polyps.

significantly increases the risk of postoperative recurrence and intensifies tissue eosinophil inflammation. Notably, RA was identified as an independent risk factor for postoperative recurrence, even when controlling for other potential variables. Our findings shed light on the clinical features of CRSwNP patients with comorbid RA, providing a detailed overview of postoperative recurrence rates within this group. This study highlights the role of RA in promoting eosinophilic infiltration in tissue and its detrimental effects on symptom severity and recurrence post-surgery in these patients.

RA is characterized as a chronic, progressive autoimmune inflammatory disease that prominently features systemic inflammation and immune cell reactivity towards joint tissues.[23] RA also significantly influences the development and prognosis of various extra-articular inflammatory conditions, impacting systems such as the nervous, respiratory, and cardiovascular systems.[24,25,30] Recent literature has found that RA can influence the nasal microbiome profile.[31] A study analyzed the prevalence of nasal Staphylococcus aureus in RA patients and reported an increased prevalence of Staphylococcus aureus nasal carriage in these individuals.[27] Staphylococcus aureus is also considered one of the common pathogens in CRSwNP, and it is commonly used as an inducer in establishing animal models.[32,33] These studies suggest a potential role for certain microorganisms in the pathogenesis of both RA and CRSwNP. Existing epidemiological survey study examining the link between CRSwNP and RA has been limited but indicative. For instance, one cross-sectional study highlighted a higher prevalence of RA among CRS patients than in controls,[34] and another found an increased incidence of CRS in patients with RA.[26] Furthermore, Shih et al[35] demonstrated a significant association between RA and various CRS phenotypes in a case-control study, noting an elevated incidence of both CRSwNP and CRSsNP among patients with pre-existing RA. Conversely, Tan et al[36] found no significant correlation between RA and subsequent CRS diagnoses, reporting that the incidence of CRS and CRSwNP in RA patients was comparable to that observed in hypertensive patients.[37] Notably, recent Mendelian randomization studies have suggested a causal relationship between RA and nasal polyps, partially mediated by the "BAFF-R for IgD^+ B cells" pathway,[38,39] further underscoring RA's role in exacerbating CRSwNP conditions. Despite these insights, research into RA's impact on the histopathology and postoperative recurrence of CRSwNP remains unexplored.

It is well established that the complex interactions between immune cells, inflammatory cells, and the cytokine composition in the immune microenvironment, along with nasal microbiota dysbiosis, are the fundamental causes of the high tissue heterogeneity and postoperative recurrence in CRSwNP.[40,41] The underlying the influence of RA on CRSwNP result from a multifaceted interplay of factors, and the potential mechanisms may involve autoimmune dysregulation, systemic inflammation, particularly eosinophilic inflammation, and the impact of RA treatments. RA is characterized by systemic autoimmune dysregulation, where the immune system erroneously targets the body's own tissues, leading to chronic inflammation and tissue damage that often extend beyond the joints to affect various other tissues.[42,43] Notably, studies in molecular biology and immunology have demonstrated elevated levels of anti-dsDNA antibodies in nasal polyp tissues,[22] suggesting a potential mechanism of pathology in CRSwNP. It is highly plausible

that in CRSwNP patients with comorbid RA, the presence of high levels of autoantibodies could damage nasal epithelial cells. This damage is likely to manifest locally within the sinonasal tract, further exacerbating chronic inflammation and compromising mucosal barrier function. Consequently, the persistent immune dysregulation in these patients may result in delayed postoperative wound healing, impaired tissue remodeling, prolonged eosinophilic inflammatory responses, and recurrent sinonasal infections. Excessive inflammatory cytokines and immune cells are central to the pathophysiology of both RA and CRSwNP.[44,45] It has been shown that synovial tissue and circulating immune cells in RA patients produce substantial amounts of pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-1, interleukin-17A, interleukin-5, and interleukin-6.[46] These cytokines play a critical role in mediating the inflammatory cascade, facilitating the recruitment of eosinophils, exacerbating tissue damage in affected areas, and sustaining ongoing eosinophilic inflammation and tissue remodeling.[47] The elevated levels of these cytokines can circulate systemically and potentially impact sinonasal tissues, thereby perpetuating inflammation in nasal and sinus passages even postoperatively. Our findings indicate that RA significantly enhances eosinophils infiltration in CRSwNP tissues, and eosinophilia is considered a major risk factor for the recurrence of CRSwNP.[11,16] Moreover, the systemic increase in pro-inflammatory cytokines due to RA can prolong inflammation and impair nasal tissue repair, creating conditions favorable for recurrent infections and inflammation. This disruption in the normal healing process is a key contributor to the recurrence of CRSwNP. Furthermore, RA can lead to nasal microbiota dysbiosis, particularly causing a significant increase in the infection and level of Staphylococcus aureus. Staphylococcus aureus infection and persistence in CRSwNP can perpetuate nasal inflammation, especially by promoting eosinophilic recruitment and general Th2 polarization, both of which play a crucial role in the pathophysiological mechanisms underlying CRSwNP recurrence.[48,49]

Treatment of RA with immunosuppressive medications and non-biologic disease-modifying anti-rheumatic drugs can disrupt immune regulation and diminish the immune system's capacity to combat infections in the sinonasal tract. These treatments can also alter immune responses both systemically and locally, potentially influencing immune cell activity within sinonasal tissues and affecting postoperative outcomes.[50] It is crucial to comprehend these complex mechanisms to refine postoperative care and improve outcomes for CRSwNP patients with comorbid RA. Additionally, further investigation is needed to better understand and address these immunological factors to minimize the risk of recurrence in this patient group.

This study has several limitations. Firstly, the participants were recruited from a single medical center, and the cohort of RA patients was relatively small, potentially introducing selection bias and limiting the generalizability of the results to a broader population. Secondly, the presence of confounding variables and unmeasured factors could influence the associations observed, complicating the interpretation of the results. Thirdly, the disease severity and treatment specifics of RA patients were not clearly documented, obscuring any direct effects these factors might have on CRSwNP recurrence. Additionally, this study was unable to establish a temporal relationship between RA exposure and the development of CRSwNP, further limiting the conclusions that can be drawn.

Conclusion

This retrospective cohort study revealed that RA might promote tissue eosinophil infiltration, potentially increasing the risk of postoperative CRSwNP recurrence. Tissue eosinophil count, percentage, and AR were identified as possible risk factors for recurrence. Patients with both CRSwNP and RA may benefit from a multidisciplinary approach that addresses both autoimmune factors and surgical challenges.

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Disclosure

There are no patents, products in development, or marketed products to declare. Authors of this manuscript have no relevant financial or other relationships to disclose.

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