



Meta-Analysis

Predictive significance of the blood eosinophilia for chronic sinusitis with nasal polyp recurrence: A systematic review and meta-analysis

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Article Info

Abstract



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Chronic sinusitis with nasal polyps (CRSwNP) is a complex inflammatory condition characterized by recurring nasal polyps, often necessitating repeated interventions. Blood eosinophilia has emerged as a potential biomarker for predicting disease recurrence. The present study aims to assess the predictive significance of blood eosinophilia for the recurrence of nasal polyps. To accomplish this objective, we employed the appropriate search keywords to explore international databases such as Web of Science, PubMed, Embase, and Scopus. Through this process, we extracted scholarly articles that assessed the prognostic value of blood eosinophilia in the recurrence of nasal polyps. The statistical software STATA (version 15) was employed, along with random and fixed-effects models, to appraise the compiled data. Nine articles met inclusion criteria, with a total sample size of 1279 individuals (569 recurrent polyp individuals and 710 non-recurrent polyp individuals). Cumulative Odds ratio analysis revealed that CRSwNP is associated with high blood eosinophile percentage compared to the non-CRSwNP group ($p=0.01$, $OR=1.26$, $95\%CI (1.15,1.36)$). The cut-off value of blood eosinophil percentage (>0.78) had relatively good, and statistically significant predictive potential. No significant publication bias was observed for the included studies. Our findings indicate that the utilization of blood eosinophils holds significant predictive value and can serve as a valuable tool for detecting recurrence in patients with CRSwNP. Based on the outcomes of our comprehensive analysis, we propose a threshold of >0.78 as a reliable indicator for assessing the probability of recurrence in CRSwNP patients.

Keywords: Chronic sinusitis, Nasal polyps, Blood eosinophilia, Predictive significance.

1. Introduction

Nasal polyps, characterized by benign growths within the nasal cavity and paranasal sinuses, pose a significant burden on individuals' quality of life due to their propensity for recurrence and associated symptoms, such as nasal obstruction, anosmia, and chronic rhinosinusitis [1]. Perennial nasal congestion, nasal obstruction, and anosmia or hyposmia are the major signs of nasal polyps. Patients with nasal polyps usually do not complain of headaches and facial pain, in contrast to those with chronic sinusitis (CRS) without nasal polyps. Nasal polyps appear as pale gray, and semitranslucent growths in the nasal cavity. Patients with CRS are phenotypically classified as CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [2]. Despite advancements in medical and surgical management, recurrence remains a common challenge, necessitating a deeper understanding of the underlying pathophysiology to enhance prognostic stratification and therapeutic approaches [3]. Amidst the multifaceted mechanisms driving nasal polyp formation and recurrence, tissue eosinophilia has emerged as a pivotal histological hallmark, raising intriguing questions about its predictive significance in determining the likelihood of disease recurrence [4].

Eosinophils, a subtype of granulocytes primarily associated with allergic and inflammatory responses, infiltrate the nasal polyp tissue, reflecting the underlying immunopathogenic processes orchestrating disease progression [5]. The intricate interplay between eosinophils, other immune cells, and the local microenvironment shapes the inflammatory milieu within nasal polyps, thereby influencing disease severity and recurrence risk [5]. Consequently, investigating the predictive implications of tissue eosinophilia holds promise in refining risk stratification algorithms and tailoring personalized therapeutic interventions for optimal patient outcomes [6].

The significance of eosinophils extends beyond their mere presence within nasal polyp tissue, encompassing their effector functions and molecular interactions driving tissue remodeling, fibrosis, and recalcitrant disease phenotypes [7]. Eosinophils secrete an array of pro-inflammatory cytokines, chemokines, and growth factors, perpetuating local inflammation, exacerbating tissue damage, and fostering a microenvironment conducive to disease recurrence [8]. Furthermore, eosinophils contribute to epithelial barrier dysfunction, mucosal edema, and angiogenesis, amplifying the pathophysiological cascade underpinning nasal polyp formation and recurrence. Thus, elucidating

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the intricate crosstalk between eosinophils and disease recurrence holds therapeutic implications for targeting specific pathways to disrupt the vicious cycle of inflammation and tissue remodeling [9].

While the association between tissue eosinophilia and nasal polyp recurrence is well-established, several caveats warrant consideration to contextualize its predictive significance accurately. Firstly, the heterogeneity in eosinophilic infiltration across nasal polyp specimens underscores the need for standardized histopathological assessment techniques to ensure reproducibility and reliability in predicting recurrence risk. Additionally, the interplay between eosinophils and other immune cells, such as T-helper type 2 lymphocytes, mast cells, and innate lymphoid cells, warrants further investigation to elucidate their synergistic or antagonistic roles in modulating disease recurrence [10]. Furthermore, the impact of systemic factors, such as comorbid allergic diseases, asthma severity, and corticosteroid responsiveness, on tissue eosinophilia and recurrence risk necessitates comprehensive patient phenotyping to tailor prognostic assessments and therapeutic interventions [10].

Therefore, the present study aims to assess the predictive value of the blood eosinophilia for nasal polyp recurrence.

2. Materials and methods

The present review study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [11].

2.1. Literature search strategy

Two authors searched for relevant English studies using the following databases: PubMed, Medline, Embase, and Science Direct. Mentioned databases were searched systematically with the keywords “blood eosinophilia”, “nasal polyp recurrence”, “predictive significance”, “disease relapse”, and “prognostic biomarker”, as well as their synonyms and abbreviations and all the possible combinations.

2.2. Study selection

Published articles written in English were included in our study by the following criteria: 1) Studies investigating the association between blood eosinophilia and nasal polyp recurrence. 2) Randomized controlled trials, prospective or retrospective cohort studies, case-control studies, and cross-sectional studies. 3) Studies involving human participants diagnosed with nasal polyps, irrespec-

tive of age, gender, or ethnicity. 4) Studies report quantitative data on blood eosinophilia, either through histopathological examination or immunohistochemical staining. 5) Studies reporting outcomes related to nasal polyp recurrence, including but not limited to recurrence rates, time to recurrence, or factors associated with recurrence. Also, exclusion criteria included: 1) Studies not investigating the association between blood eosinophilia and nasal polyp recurrence. 2) Animal studies, in vitro studies, review articles, case reports, editorials, and letters to the editor. 3) Studies lacking sufficient data on blood eosinophilia or nasal polyp recurrence outcomes. 4) Studies focusing solely on treatment interventions without assessing the predictive significance of blood eosinophilia for recurrence. 5) Studies published in languages other than English, due to limitations in language proficiency for analysis. 6) Studies with inadequate methodological quality or high risk of bias, as determined by predefined quality assessment criteria.

2.3. Screening and data extraction

The results of our search were screened by two independent authors considering the inclusion and exclusion criteria. Another two independent authors independently extracted the data from the included studies. The following data were extracted: first author, authors’ country, year of publication, study design, sample size, gender, age, cut-off value (%), 95% CI cut-off value, and odds ratio of eosinophil (%).

2.4. Risk of bias in individual studies (Quality assessment)

The quality of the included studies was assessed by the Newcastle - Ottawa Quality Assessment Scale (adapted for cross-sectional studies). All the included articles were evaluated in three domains, including selection, comparability, and outcome. Finally, the quality of each of the included studies was reported by a score (Maximum score = 10). Studies with a score of 7 or 8 were considered as a study with a low bias risk. Studies that scored 6 points were considered to have a medium risk of bias. Studies with 5 or fewer points as their score were considered to have a high bias risk. High-risk studies for bias with scores lower than 4 points were excluded from our study (Table 1).

2.5. Risk of bias across studies

The Egger test and Begg's Funnel plots assessed the

Table 1. Risk of bias in individual studies.

Reference	Type of Study	Selection				Comparability			Outcome			Total
		1	2	3	4	1	2	3	1	2	3	
Brescia G [12]	Retrospective	*	*	*		*			*	*		6
Du K [13]	Retrospective	*			**	*			**			6
Lu PC [14]	Prospective cohort study	*	*	*	*	*			*	*	*	8
Virkkula P [15]	Retrospective	*	*			*			**			5
Wang X [16]	Prospective cohort study	*	*	*		*			**			6
Nakayama T [17]	Prospective cohort study	*	*		**	*			**	*		8
Cengiz AB [18]	Retrospective	*	*	*	*	*			*	*		7
Guo M [19]	Retrospective case series	*	*	*		*			**	*	*	8
Zhang J [20]	Retrospective	*	*	*	*	*			*	*		7

publication bias. P values under 0.05 were taken into consideration for heterogeneity.

2.6. Statistical analysis

Stata version 15 was used to calculate the effect size and the 95% CI. Moreover, the publication bias was assessed by calculating the P-value with Stata software. We measured the heterogeneity of each group using the inconsistency index (I^2). An I^2 greater than 50% or P lower than 0.05 is recognized as significant heterogeneity. If the heterogeneity was high, a random-effect model was used to calculate the pooling effect and 95% CI. Otherwise, the fixed effect was used. Two-by-two tables were generated for various blood eosinophilia cut-off scores, with the primary outcome being the risk of recurrence.

3. Results

3.1. Study selection

After using the aforementioned keywords in the initial search, a total of 1862 studies were found. At first, we eliminated 596 studies that were duplicated from the list of included research. After a title and abstract screening, 1164 studies were excluded from our study. Following a comprehensive text assessment and screening of 102 papers, 93 articles were deemed ineligible for inclusion in our study based on the inclusion and exclusion criteria. Ultimately, Nine articles met the inclusion criteria, with a total sample size of 1279 individuals (569 recurrent polyp individuals and 710 non-recurrent polyp individuals) (Fig. 1) (Table 2).

The cut-off value of blood eosinophil percentage (>0.78) had relatively good, and statistically significant (vigorous), predictive potential (Fig. 2).

Cumulative Odds ratio analysis revealed that CRSwNP is associated with high blood eosinophile percentage compared to the non-CRSwNP group ($p=0.01$, $OR=1.26$,

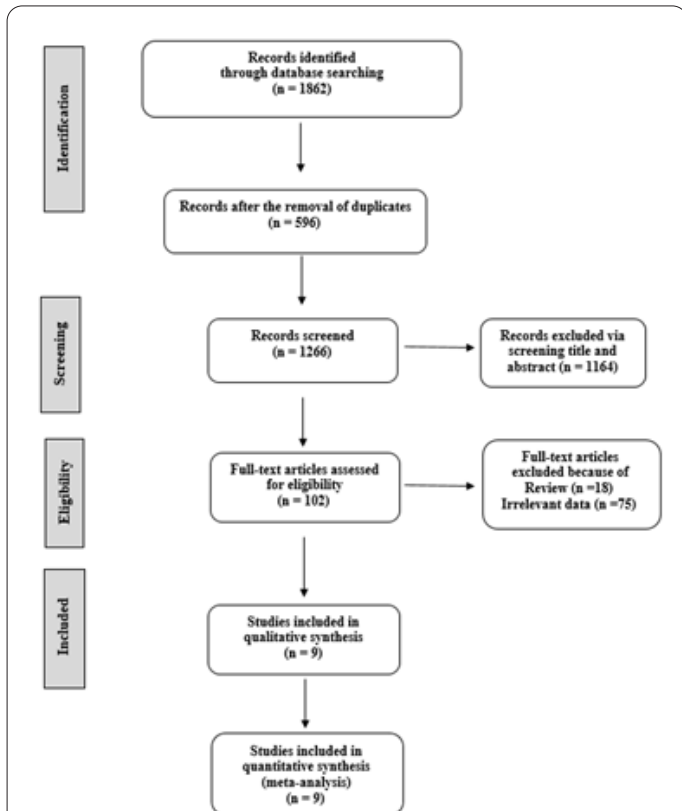


Fig. 1. PRISMA flow diagram showing the articles selection process.

95%CI (1.15,1.36) (Fig. 3).

3.2. Risk of bias between studies

No significant publication bias was observed for included studies using Begg's ($P = 0.052$) test. Figure 4 re-

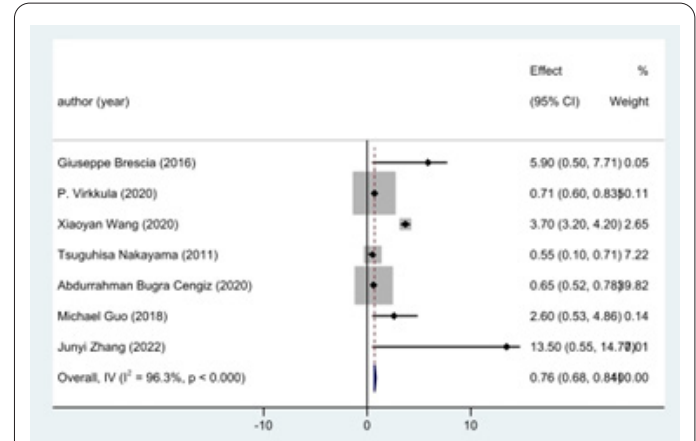


Fig. 2. The cut-off value of blood eosinophil percentage with a 95% confidence interval (based on a random model).

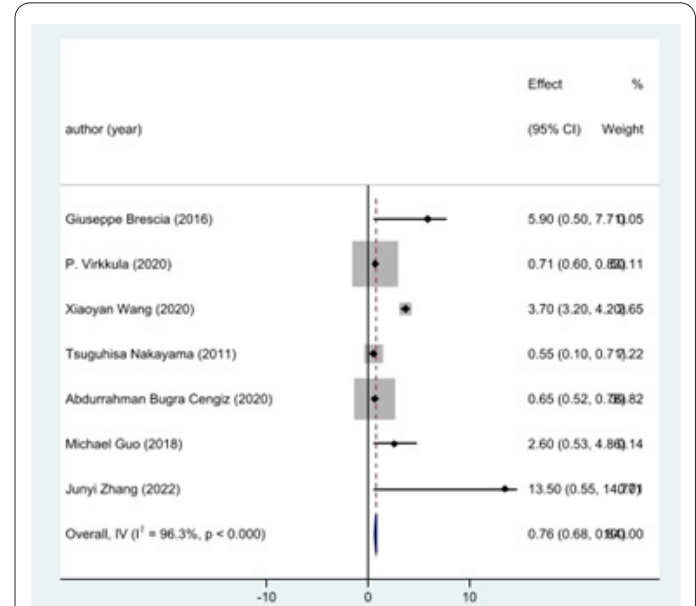


Fig. 3. Eosinophile percentage in the CRSwNP group compared to non-CRSwNP group with a 95% confidence interval (based on a random model).

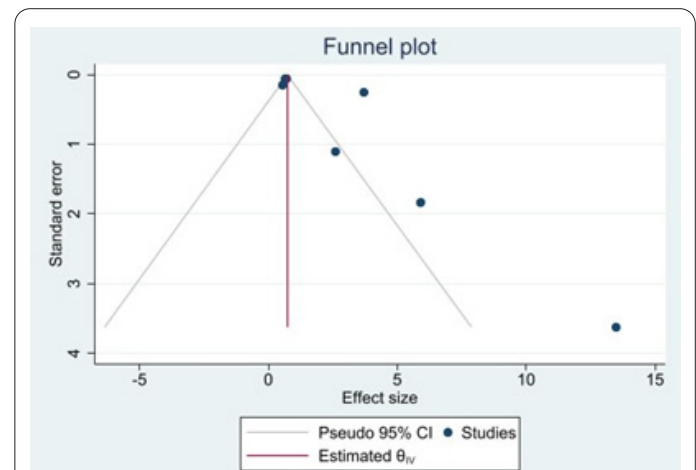


Fig. 4. The funnel plot of the meta-analysis's included studies to evaluate any possible publication bias.

Table 2. Characteristics of the included studies.

Reference	Country	Recurrent polyp individuals	Non-Recurrent polyp individuals	Recurrent polyp Age	Non-Recurrent polyp Age	Study design	Cut-off value (%)	95% CI value	Odds ratio of Eosinophil (%)	95% CI off value
Brescia G 2017 [12]	Italy	57	223	-	-	Retrospective	5.9	0.5-7.71	2.52	1.09-5.88
Du K 2021 [13]	China	28	68	47.1±13.4	49.3±14.3	Retrospective	-	-	1.164	1.0511.29
Lu PC 2020 [14]	Taiwan	9	49	48 (43.5-54.5) IQR	48 (36-57) IQR	Prospective cohort study	-	-	1	1-1
Virkkula P 2020 [15]	Finland	47	34	45.6 (35.3-55.7) IQR	57.3 (43.8-64.2) IQR	Retrospective	0.71	0.6-0.83	-	-
Wang X 2020 [16]	China	169	144	46.6 ± 4.1	46.1 ± 5.7	Prospective cohort study	3.7	3.2-4.2	1.57	1.31-1.77
Nakayama T 2011 [17]	Japan	68	21	48.2±13.3	42.6±12.4	Prospective cohort study	0.553	0.104-0.71	3.47	1.65-7.29
Cengiz AB 2022 [18]	Turkey	144	66	43.95 ± 12.2	46.3 ± 12.3	Retrospective	0.653	0.5240.782	4.26	1.56-11.61
Guo M 2018 [19]	Canada	11	65	52± 14.6	52.36± 12.65	Retrospective case series	2.6	0.53-4.86	5.12	0.62-42.58
Zhang J 2023 [20]	China	32	40	41.1 ± 15.0	38.4 ± 17.5	Retrospective	13.5	0.5514.77	-	-

presents the risk of publication bias among studies based on the above-mentioned test.

4. Discussion

The objective of the current study is to assess the predictive significance of blood eosinophilia for the recurrence of nasal polyps. A crucial finding of our research is the establishment of a threshold value (>0.78) for blood eosinophil percentage, which exhibits a commendable level of predictive potential and statistical significance. This discovery equips healthcare professionals with a valuable tool for stratifying risk and making prognostic assessments in patients with nasal polyps. Importantly, our meta-analysis underscores the need to consider systemic inflammatory markers, such as blood eosinophil percentage, in addition to traditional histopathological evaluations of tissue eosinophilia. This comprehensive approach enhances predictive accuracy and refines therapeutic strategies. The establishment of a specific threshold value for blood eosinophil percentage contributes precision to prognostic evaluations and facilitates tailored treatment approaches for individuals with nasal polyps. Clinicians can employ this threshold to stratify patients based on risk, customize treatment strategies, and monitor disease progression over time. For instance, patients with blood eosinophil percentage exceeding the identified cut-off may benefit from more aggressive medical therapy, including biologic agents targeting specific inflammatory pathways implicated in eosinophilic inflammation.

The observed correlation between CRSwNP and a high blood eosinophil percentage is consistent with the well-established role of eosinophilic inflammation in the progression and recurrence of the disease [21]. Eosinophils play a significant role in type 2 inflammation by orchestrating a series of pro-inflammatory cytokines and chemokines that sustain mucosal inflammation, tissue remodeling, and the formation of polyps. Consequently, elevated levels of eosinophils in the blood can be utilized as a surrogate marker for the underlying immunopathogenic processes that drive CRSwNP, indicating the potential usefulness of this biomarker in guiding treatment decisions and predicting disease outcomes [5, 22].

Several relative studies have contributed to our understanding of eosinophilic inflammation and its predictive value for nasal polyp recurrence, thereby complementing the findings of our study.

One such study by Lou et al. (2015) investigated the role of tissue eosinophilia in predicting recurrence of nasal polyps. They found that higher levels of tissue eosinophilia were associated with increased likelihood of polyp recurrence. This aligns with our study's emphasis on the predictive potential of eosinophilic markers. However, while our study focused on blood eosinophil percentage, Lou et al. focused on tissue eosinophilia, indicating the multifaceted nature of eosinophilic inflammation assessment [4].

Another relevant study by Gevaert et al. (2018) [23] explored the utility of blood eosinophil count in predicting recurrence after ESS in patients with CRSwNP. They observed that elevated blood eosinophil counts were associated with a higher risk of recurrence. This finding corroborates our study's identification of a specific cut-off value (>0.78) for blood eosinophil percentage as a predictive marker for nasal polyp recurrence. Both studies highlight the importance of systemic inflammatory markers, parti-

cularly blood eosinophils, in prognostic assessment and treatment decision-making.

A meta-analysis conducted by McHugh et al. (2018) [24] further supports the significance of eosinophils as a predictive marker for recurrence in patients with CRS. The proposed threshold value of >55 eosinophils per high-power field presents a reliable indicator for predicting the likelihood of recurrence of eosinophilic chronic rhinosinusitis (ECRS). This highlights the importance of obtaining sinus tissue samples for eosinophil quantification in clinical practice.

However, it is essential to acknowledge the limitations of the current study and other similar studies. Variability in methodological quality across studies and differences in the definition of recurrence may contribute to heterogeneity in the findings. Additionally, the definition of recurrence as the presence of at least grade 1 polyps may not fully capture the complexity of disease progression and recurrence.

5. Conclusion

In conclusion, the findings of the study underscore the predictive potential of blood eosinophil percentage for nasal polyp recurrence in patients with CRSwNP. The identification of a specific cut-off value enhances prognostic accuracy and facilitates personalized treatment approaches. By integrating blood eosinophil percentage into clinical practice, clinicians can optimize treatment outcomes and minimize the burden of recurrent disease on affected individuals. Further research addressing methodological limitations and refining definitions of recurrence is warranted to enhance our understanding and management of CRSwNP.

Conflict of interests

The author has no conflicts with any step of the article preparation.

Consent for publications

The author read and approved the final manuscript for publication.

Ethics approval and consent to participate

No human or animals were used in the present research.

Informed consent

The authors declare not to use any patients in this research.

Availability of data and material

All data are available and they can be sent to the accredited authors.

Authors' contributions

The author has performed all the work in this meta-analysis study.

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Non

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