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RISK FACTORS FOR RECURRENCE OF NASAL POLYPS IN CASES OF CHRONIC RHINOSINUSITIS AFTER ENDOSCOPIC SINUS SURGERY: A NARRATIVE REVIEW

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Contributions:
A Study design/planning
B Data collection/entry
C Data analysis/statistics
D Data interpretation
E Preparation of manuscript
F Literature analysis/search
G Funds collection

Abstract

Introduction: Chronic rhinosinusitis (CRS) is a persistent inflammatory disease of the nasal mucosa and paranasal sinuses, classified into phenotypes with (CRSwNP) and without (CRSsNP) nasal polyps. A key limitation of endoscopic sinus surgery (ESS) for CRSwNP is the frequent recurrence of polyps. This narrative review aims to summarize current evidence on risk factors for polyp recurrence after ESS.

Material and methods: All relevant publications published from 2019 to 2024 were retrieved from PubMed based on the keywords *chronic rhinosinusitis*, *endoscopic sinus surgery*, and *nasal polyps*. Exactly 47 papers were identified.

Results: A number of risk factors for polyp recurrence in CRSwNP patients following prior ESS were identified. Most highlight the significant number of relapses in patients with asthma, allergic rhinitis, eosinophilia, aspirin hypersensitivity, smoking, non-compliance with post-procedure recommendations, prior sinus surgery, and elevated levels of inflammatory factors (interleukins: IL-5, IL-10, and IL-6).

Conclusions: Recognition of these risk factors and incorporation of biomarker assessment may improve patient stratification and enable tailored postoperative management. Further studies are needed to validate these predictors and develop effective strategies to reduce recurrence rates in CRSwNP patients.

Keywords: nasal polyps • chronic rhinosinusitis • endoscopic sinus surgery

CZYNNIKI RYZYKA NAWROTU POLIPÓW NOSA U OSÓB Z PRZEWLEKŁYM ZAPALENIEM ZATOK PRZYNOSOWYCH PO ENDOSKOPOWEJ OPERACJI ZATOK – PRZEGLĄD NARRACYJNY

Streszczenie

Wprowadzenie: Przewlekłe zapalenie zatok przynosowych (CRS) to przewlekła choroba zapalna błony śluzowej nosa i zatok przynosowych, klasyfikowana jako fenotyp z polipami nosa (CRSwNP) oraz bez polipów nosa (CRSsNP). Podstawowym ograniczeniem endoskopowej chirurgii zatok przynosowych (ESS) w przypadku CRSwNP jest częsty pooperacyjny nawrót polipów. Niniejszy przegląd narracyjny ma na celu podsumowanie aktualnych dowodów naukowych dotyczących czynników ryzyka nawrotu polipów po ESS.

Materiał i metody: Wszystkie istotne publikacje opublikowane w latach 2019–2024 zostały wyszukane w bazie PubMed na podstawie słów kluczowych: *chronic rhinosinusitis*, *endoscopic sinus surgery*, *nasal polyps*. Wybrano dokładnie 47 artykułów.

Wyniki: Naukowcy zidentyfikowali wiele czynników ryzyka nawrotu polipów u pacjentów z CRSwNP po wcześniejszej ESS. Nawroty polipów większość autorów zaobserwowała u pacjentów: z astmą, alergicznym nieżytem nosa, eozynofilią, nadwrażliwością na ASA, palących tytoń, nieprzestrzegających zaleceń pooperacyjnych, z wcześniejszą endoskopową chirurgią zatok przynosowych oraz podwyższonym poziomem czynników zapalnych – zwłaszcza interleukin: IL-5, IL-10 i IL-6.

Wnioski: Rozpoznanie tych czynników ryzyka i włączenie oceny biomarkerów może poprawić stratyfikację pacjentów i umożliwić dostosowane postępowanie pooperacyjne. Konieczne są dalsze badania w celu walidacji tych czynników predykcyjnych i opracowania skutecznych strategii zmniejszania częstości nawrotów u pacjentów z CRSwNP.

Słowa kluczowe: przewlekłe zapalenie zatok przynosowych • endoskopowa chirurgia zatok przynosowych • polipy nosa

Key to abbreviations	
AAO-HNS	American Academy of Otolaryngology – Head and Neck Surgery
AERD	aspirin-exacerbated respiratory disease
ALCAM	activated leukocyte cell adhesion molecule
ASA	acetylsalicylic acid
BAFF	B cell-activating factor
BMI	Body Mass Index
CLCs	Charcot–Leyden crystals
CRS	chronic rhinosinusitis
CRSwNP	chronic rhinosinusitis *with* nasal polyps
CRSsNP	chronic rhinosinusitis *sans* nasal polyps
ECP	eosinophil cationic protein
EPOS	European Position Paper on Rhinosinusitis and Nasal Polyps
ESS	endoscopic sinus surgery
IgE	Immunoglobulin E
IL	interleukin
MLK	modified Lund–Kennedy
MLM	modified Lund–Mackay
MMP	matrix metalloproteinases
MUC	mucin
NOS	nitric oxide synthase
NSAID	non-steroidal anti-inflammatory drug allergy
sIgE	specific Immunoglobulin E
sST2	soluble ST2
TIMP	tissue inhibitors of metalloproteinases
Treg	regulatory T
TSLP	thymic stromal lymphopoietin
TSLPR	thymic stromal lymphopoietin receptor

Introduction

Chronic rhinosinusitis (CRS) is characterized by persistent inflammation of the nasal mucosa and paranasal sinuses [1]. Based on the presence of nasal polyps, CRS is classified into two phenotypes: chronic rhinosinusitis *with* nasal polyps (CRSwNP, accounting for approximately 20% of CRS cases) and chronic rhinosinusitis *without* (*sans*) nasal polyps (CRSsNP) [2,3]. The 2020 European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) [4] further categorizes CRS into primary and secondary forms, and within these, into localized (unilateral) and diffuse (bilateral) types based on polyp location. Additionally, CRS is endotyped into predominant type 2 inflammation and non-type 2 inflammation (absence of type 2 markers), with CRSwNP generally classified as diffuse and driven by type 2 inflammation [4]. CRSwNP occurs more frequently in men, although the disease tends to follow a more severe course in women. CRS is characterized by a high rate of recurrence and a heterogeneous clinical course [2,3].

Common symptoms of rhinosinusitis include nasal obstruction, persistent rhinorrhea, nasal swelling and congestion, hyposmia, sinus pressure, facial pain, headaches, and fatigue. Secondary complications such as nasal polyps can exacerbate symptoms and complicate treatment [5–8]. In pediatric populations, symptoms may differ and often include cough, irritability, fatigue, halitosis, periorbital swelling and redness, as well as thick yellow-green nasal or postnasal discharge. Children are also at increased risk for progression from acute to chronic rhinosinusitis [5–7].

Beyond physical symptoms, CRS significantly impacts mental health, contributing to reduced concentration, sadness, anxiety, sleep disturbances, and social discomfort. This adversely affects daily functioning, self-esteem, and parental well-being in affected children [2,6]. Patients, especially those with anosmia, face a higher risk of depression [2].

Diagnostic criteria established by the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) in 2015 (**Table 1**) require the presence of two or more cardinal symptoms (facial pain/pressure/fullness, hyposmia/anosmia, nasal obstruction, and mucopurulent nasal drainage) persisting for at least 12 weeks, alongside objective evidence of inflammation (such as purulent mucus or edema in the middle meatus or anterior ethmoid

Table 1. Diagnostic criteria for chronic rhinosinusitis (CRS) as established by the American Academy of Otolaryngology – Head and Neck Surgery [9,10]

Criterion	Details
Symptoms (≥2 of the 4 listed for ≥12 weeks)	Facial pain/pressure/fullness Hyposmia/anosmia (reduced sense of smell) Nasal obstruction Anterior or posterior mucopurulent nasal drainage
Documented inflammation (at least 1 of the 3 listed)	Purulent mucus or edema in the middle meatus or anterior ethmoid region Presence of nasal polyps in the nasal cavity or middle meatus Evidence of inflammation on radiographic imaging (e.g., CT scan)

region, presence of nasal polyps, or radiographic signs of inflammation) [9,10].

The inflammatory profile of CRS varies across geographic regions. Type 2 inflammation, characterized by local eosinophil infiltration and elevated IgE and cytokines (IL-4, IL-5, IL-13), predominates in Western populations and is frequently associated with asthma. In contrast, Asian populations more commonly exhibit type 1 and type 3 inflammation, with lower eosinophil counts but elevated TNF-α and IL-17 levels [3,11,12].

Endoscopic sinus surgery (ESS) remains the cornerstone treatment for patients unresponsive to pharmacological therapy, including intranasal and systemic corticosteroids. ESS is widely performed regardless of immune response type. However, nasal polyp recurrence after surgery is common and poses a significant clinical challenge. Identifying factors that contribute to polyp recurrence is critical for optimizing treatment and improving long-term outcomes [2,13,14].

This narrative review summarizes current knowledge regarding risk factors associated with nasal polyp recurrence following ESS, emphasizing the potential clinical and pathological predictors.

Material and methods

The aim of this review was to identify and summarize potential risk factors for nasal polyp recurrence following endoscopic sinus surgery in patients diagnosed with chronic rhinosinusitis with nasal polyps.

Eligibility criteria

We included studies published within the last 5 years, focusing on CRSwNP, its pathogenesis, and factors influencing nasal polyp recurrence after ESS. All types of observational studies were considered eligible for inclusion.

Search strategy

A comprehensive literature search was conducted using the PubMed database. The following keywords and their combinations were used: *chronic rhinosinusitis* (2,649 results), *endoscopic sinus surgery* (2,293 results), and *nasal polyps* (1,701 results). The final search and review of source texts was performed on 3 January 2025.

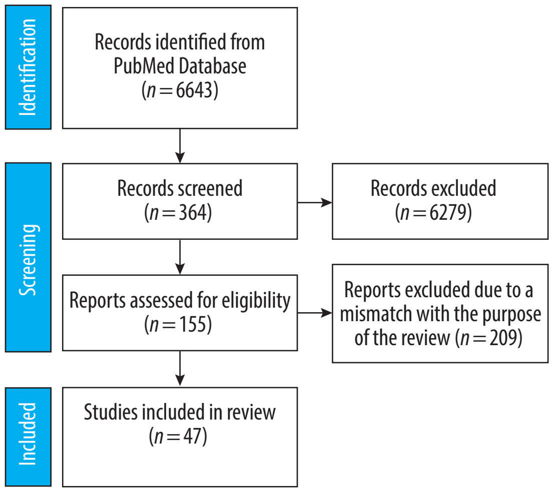

Figure 1. PRISMA flow diagram of the study selection process

Inclusion criteria were: publication within the last 5 years, availability of full text, English language, relevance to the topic, ethical approval (for original research), and high methodological quality. Exclusion criteria comprised older publications, animal studies, pharmacological models, non-English articles, and studies lacking ethical approval or deemed unreliable.

Data collection

Initially, titles and abstracts of retrieved papers were screened for relevance. A total of 6,643 articles were initially identified from the PubMed database between 2019 and 2024. After removing duplicates and screening based on title relevance, 364 articles remained. Abstract review further narrowed this to 155 studies assessed for methodological quality and relevance to the inclusion criteria. Subsequently, full-text articles were reviewed, resulting in the selection of 47 studies that were most pertinent to the review's focus.

Extracted data included diagnostic criteria for CRSwNP, insights into its pathogenesis, details on ESS, and reported risk factors for polyp recurrence following surgery.

The study selection process is summarized in **Figure 1**.

Results

Recurrence of nasal polyps following ESS in patients with chronic rhinosinusitis with CRSwNP occurs frequently. Multiple studies have investigated the clinical and biological factors influencing the risk of polyp recurrence.

Clinical risk factors

Several studies have identified key clinical predictors for polyp recurrence. Mohamed et al. [15] highlighted smoking, concomitant asthma, allergy, previous sinus surgery, aspirin sensitivity, and nasal anatomical variations as significant risk factors in their cohort of patients resistant to medical treatment. Similarly, Fageeh et al. [16] found asthma and smoking to be strongly associated with polyp recurrence, while factors such as septal deviation, age, gender, and BMI showed no correlation. Alqahtani et al. [5] reported that recurrent upper respiratory tract infections, nasal allergies, smoking, and impaired sinus ventilation (including turbinate hypertrophy, nasal polyps, and septal deviation) were significantly associated with CRSwNP recurrence. Correspondingly, Mamat Nasir et al. [8] identified smoking and nasal allergies as important contributors to relapse risk in their patient cohort and Mullol et al. [2] additionally highlighted bronchiectasis as a risk factor.

Calvanese et al. [17] found that asthma, hypersensitivity to acetylsalicylic acid (ASA), and eosinophilia level were significantly associated with polyp recurrence and involvement of multiple sinus sites, but there was no link to sex, age, or preoperative eosinophil count. Bouatay et al. [18] similarly emphasized asthma and ASA intolerance, as well as patient non-compliance with intranasal steroid therapy, as key factors influencing recurrence risk. Abuduruk et al. [19] additionally noted the effect of surgery extent, patient adherence to postoperative care, IL-5 expression, and T2 inflammatory profile on recurrence.

The impact of smoking on recurrence was further explored by Cavaliere et al. [20], who found higher rates of polyp recurrence in nonsmokers and former smokers than in current smokers, suggesting complex interactions between smoking status and disease progression.

Chen et al. [21] identified metabolic syndrome as an independent risk factor, with recurrence risk increasing with the number of metabolic components present. Yuan et al. [22] reported increased polyp recurrence in CRSwNP patients with rheumatoid arthritis, emphasizing the role of systemic inflammation.

Microbiome and inflammatory cytokines

Gan et al. [23] demonstrated that neutrophilic inflammation, characterized by elevated neutrophil and eosinophil counts and increased expression of IFN-γ, IL-17A, IL-17E, and IL-18, correlated with polyp recurrence and was linked to dysbiosis with increased *Staphylococci* and decreased *Corynebacterium* species in recurrent cases. Peng et al. [24] identified preoperative rectal carriage of *Staphylococcus aureus* as a significant risk factor, along with asthma, NSAID allergy, and prior ESS. Yu et al. [25] further underlined the role of neutrophil infiltration and elastase activity as markers of severe disease and recurrence.

Biomarkers predicting recurrence

Beyond clinical risk factors, numerous biomarkers have been examined for their predictive value in recurrence. Bai et al. [26] reported that elevated eosinophil cationic protein (ECP), interleukin-5 (IL-5) expression, higher modified Lund–Mackay (MLM) and modified Lund–Kennedy (MLK) scores, as well as anti-dsDNA IgG, were strongly associated with recurrence risk. These findings suggest that both radiologic and immunologic markers may help identify patients requiring intensified postoperative care.

Similarly, Viksne et al. [27] reported increased expression of IL-4, IL-6, IL-7, IL-10, and IL-12 in the subepithelial connective tissue of polyps from patients with recurrent CRSwNP, accompanied by decreased cytokine concentrations in the epithelium compared to controls. IL-6 showed a strong correlation with other cytokines and the proliferation marker Ki-67, suggesting its role as a predictor of polyp recurrence. Similarly, IL-4, IL-7, IL-10, and IL-12 correlated with Ki-67, indicating their potential involvement in polyp cell proliferation.

Lin et al. [28] also highlighted the prognostic significance of tissue and serum biomarkers in predicting polyp recurrence after ESS. Their study demonstrated that higher levels of tissue eosinophils, ECP, serum IgE, and interleukin-5 were associated with an increased risk of recurrence. Moreover, they pointed to the role of postoperative factors, such as infection and changes in the nasal cavity environment, in influencing surgical outcomes.

Wang et al. [29] found that B7-H4 mRNA expression levels were significantly elevated in CRSwNP patients, particularly in those with recurrent polyps, correlating with eosinophilia and suggesting B7-H4 as a potential marker for predicting postoperative recurrence. Deng et al. [30] demonstrated higher expression of SERPINB10 in recurrent CRSwNP tissues compared to primary cases and controls, with a positive correlation between SERPINB10 and eosinophilic inflammation, indicating its potential as a biomarker for polyp recurrence.

Niu et al. [31] identified increased serum levels of CSF1R and CDC42, and decreased DHRS9, in recurrent CRSwNP patients compared to non-recurrent cases. CSF1R expression was particularly linked to M2 macrophage polarization and cytokine production, which may contribute to recurrence risk. Deng et al. [32] reported elevated serum and tissue S100A8 concentrations in CRSwNP patients, especially in those with recurrence, correlating with eosinophil levels and suggesting its utility as a predictor of surgical outcomes.

Exosomal miRNAs have also been implicated in recurrence. Chen et al. [33] found that increased expression of miR-3174 and miR-192-3p was associated with higher recurrence risk, while Wang et al. [34] identified altered expression of miR-141-3p and miR-3679-5p in serum exosomes of CRSwNP patients, with greater changes observed in eosinophilic phenotypes.

Table 2. Summary of research findings [15–29,32,34–37,39,40,43,44]

Author, year	Detected risk factors	Recurrence rate in the study [%]	Follow-up period
Bai et al., 2022 [26]	Cationic eosinophil proteins, IL-5 expression, pre-ESS MLM, anti-dsDNA IgG, asthma	39.4	2–5 years
Bouatay et al., 2024 [18]	Asthma, ASA sensitivity, compliance with post-procedure recommendations, allergic rhinitis, Samter's triad	20.7	3 years (avg., min. 12 months)
Calvanese et al., 2024 [17]	Asthma, eosinophilia, ASA sensitivity	24.0	2 years
Chen et al., 2022 [43]	Increased CLCs expression	30.0	2 years
Chen et al., 2024 [21]	Metabolic syndrome	41.8	>2 years
Deng et al., 2024 [32]	S100A8 expression	23.3	no data
Fageeh et al., 2023 [16]	Asthma, smoking, bilateral polyps, average polyp grade, Lund Mackay score	51.5	2 years
Gan et al., 2021 [23]	Sinus microbiome composition, inflammatory cytokines, eosinophils and neutrophils concentration in polyp tissue	15.6	1 year
Gao et al., 2024 [44]	Increased sIgE, IL-6 and decreased Treg level	24.2	1 year
Guerra et al., 2021 [36]	MMP-2, MMP-7, MMP-9 and TIMP-1, TIMP-2 expression, asthma, non-allergic rhinitis	37.8	3 years
Kidoguchi et al., 2020 [39]	Increased NOS expression	25.7	no data
Lin et al., 2024 [27]	Preoperative tissue eosinophil percentage, ECP, IgE levels, IL-5 expression, postoperative nasal environment	19.5	6 months
Liu et al., 2020 [35]	MUC5AC, MUC5B, MUC2 expression	23.2	6 months – 1 year
Mohamed et al., 2023 [15]	Smoking, asthma, allergy, ASA sensitivity, septal deviation, prior sinus surgery, turbinate hypertrophy	15.0	6 months
Peng et al., 2023 [24]	Rectal S. aureus carriage, asthma, NSAID allergy, previous ESS	36.3	2 years
Viksne et al., 2022 [28]	IL-4, IL-6, IL-7, IL-10, IL-12, Ki-67 expression	no data	no data
Wang et al., 2022 [29]	mRNA B7-H4 expression	no data	no data
Wang et al., 2024 [37]	Upregulation of miR-141-3p and downregulation of miR-3679-5p	44.8	12–31.5 months
Yu et al., 2022 [25]	Human neutrophil elastase level, serum eosinophil count, IL-10 expression, younger age	25.7	1 year
Yuan et al., 2024 [22]	Rheumatoid arthritis	22.6	2 years
Zhang et al., 2022 [40]	Increased level of IL-33 and sST2	28.2	3 years
Zhang et al., 2022 [33]	Increased ALCAM expression	29.1	>2 years

Tissue remodeling and immune regulation

Alterations in tissue remodeling markers have a significant impact on the risk of polyp recurrence in patients with CRSwNP. Liu et al. [35] examined mucin expression (MUC2, MUC5AC, MUC5B) in nasal polyp tissues, finding that elevated mucin levels correlated with polyp recurrence, while downregulation was negatively associated with relapse rates. Guerra et al. [36] showed increased expression of matrix metalloproteinases (MMP-2, MMP-7, MMP-9) and decreased tissue inhibitors of metalloproteinases (TIMP-1, TIMP-2) in CRSwNP patients, especially in those with asthma and nonallergic rhinitis, which correlated with higher recurrence rates.

Zhang et al. [37] demonstrated that serum and tissue levels of activated leukocyte cell adhesion molecule (ALCAM) were significantly elevated in CRSwNP patients, particularly in eosinophilic phenotypes, and correlated positively with eosinophil counts and postoperative relapse risk. Soon after, Zhang et al. [38] also reported increased expression of B cell-activating factor (BAFF) in recurrent CRSwNP patients, which was associated with higher eosinophil percentages and polyp recurrence.

Table 3. Summary of research findings including the number of patients with recurrent or non-recurrent CRSwNP who completed the whole follow-up [30,31,33,37,41,42]

Author, year	Detected risk factors	Number of patients included
Chen et al., 2024 [33]	Upregulation of miR-3174 and downregulation of miR-192-3p	8 RG – 4 NRG – 4
Deng et al., 2022 [30]	SERPINB10 expression	140 (60 – CRSwNP; 40 – CRSsNP; 40 – HC) RG – 24 NRG – 36
Niu et al., 2024 [31]	CSF1R expression	Discovery cohort: 16 RG – 6 NRG – 10 Validation cohort: 75 RG – 24 NRG – 51
Wang et al., 2022 [42]	Increased eotaxin, G-CSF, IFN-α, IL-13, IL-17A, IL-5, MCP-1, and RANTES level	72 RG – 36 NRG – 36
Wen et al., 2021 [41]	Increased YKL-40 expression	160 (120 – CRSwNP; 40 – HC) RG – 40 NRG – 80
Zhang et al., 2022 [37]	Increased BAFF expression	160 (80 – CRSwNP; 40 – CRSsNP; 40 – HC) RG – 40 NRG – 40

Note: CRSwNP, chronic rhinosinusitis with nasal polyps; CRSsNP, chronic rhinosinusitis without nasal polyps; RG, recurrent group (CRSwNP); NRG, non-recurrent group (CRSwNP); HC, healthy controls

Table 4. Summary of other findings included in the review

Authors	Conclusion
Niu et al., 2023 [31] Zhu et al., 2022 [1]	M2 macrophages play a role in the development of CRSwNP by modulating immune responses and contributing to tissue remodeling
AlBloushi et al., 2024 [11] Barroso et al., 2023 [9] Fokkens et al., 2020 [4] Klingler et al., 2021 [3] Mullol et al., 2022 [2]	Chronic rhinosinusitis with nasal polyps and asthma frequently exhibit similar type 2 immunopathology, with epithelial barrier dysfunction observed in both conditions. Additionally, about 25% of individuals with CRSwNP also have asthma (compared to 5% in general population)
Laidlaw et al., 2021 [12]	Aspirin/nonsteroidal anti-inflammatory drug-exacerbated respiratory disease (AERD) is a well-established phenotype of CRSwNP that often coexists with asthma and is characterized by a severe clinical course
Martin-Jimenez et al., 2023 [13]	Surgical approaches involving extensive resection of the sinus bony structures (reboot surgery) and treatment of the mucosal lining of the nasal cavity (mucoplasty), along with improved surgical outcomes and reduced polyp recurrence, contribute to a better quality of life for patients
Barroso et al., 2023 [9] Miglani et al., 2023 [14]	Biological agents (including dupilumab, mepolizumab, and omalizumab) act as alternatives to ESS, but their effectiveness in reducing polyp size is significantly lower compared to ESS

Kidoguchi et al. [39] linked increased expression of nitric oxide synthase 2 (NOS2) and its gene polymorphisms with a higher risk of postoperative recurrence, particularly in eosinophilic CRSwNP. Zhang et al. [40] found elevated serum levels of IL-33 and soluble ST2 (sST2) in eosinophilic CRSwNP patients, which correlated with eosinophilia and recurrence risk, demonstrating their potential as predictive biomarkers.

Wen et al. [41] identified YKL-40 as a mediator associated with type 2 inflammation and polyp recurrence, showing higher levels in recurrent eosinophilic CRSwNP patients and correlation with eosinophil counts. Wang et al. [42] evaluated a panel of cytokines and found elevated serum levels of eotaxin, G-CSF, IFN-α, IL-13, IL-17A, IL-5, MCP-1, and RANTES in recurrent CRSwNP patients. Among these, eotaxin and RANTES showed strong predictive value for recurrence.

Table 5. Summary of the most common detected risk factors for polyp recurrence in CRSwNP patients

Authors	Detected factor
Abuduruk et al., 2024 [19] Alshehri et al., 2021 [7] Bai et al., 2022 [26] Bouatay et al., 2024 [18] Calvanese et al., 2024 [17] Cavaliere et al., 2024 [20] Fageeh et al., 2023 [16] Guerra et al., 2021 [36] Mohamed et al., 2023 [15] Moreno-Jimenez et al., 2025 [45] Mullol et al., 2022 [2] Peng et al., 2023 [24] Rizzi et al., 2023 [46]	Asthma
Abuduruk et al., 2024 [19] Alqahtani et al., 2023 [5] Alshehri et al., 2021 [7] Bai et al., 2022 [26] Bouatay et al., 2024 [18] Calvanese et al., 2024 [16] Ma et al., 2022 [47] Mamat et al., 2022 [8] Mohamed et al., 2023 [15]	Allergy (including allergic rhinitis, eosinophilia)
Abuduruk et al., 2024 [19] Bouatay et al., 2024 [18] Calvanese et al., 2024 [17] Mohamed et al., 2023 [15] Mullol et al., 2022 [2] Peng et al., 2023 [24]	ASA sensitivity
Alqahtani et al., 2023 [5] Fageeh et al., 2023 [16] Mamat et al., 2022 [8] Mohamed et al., 2023 [15]	Smoking
Abuduruk et al., 2024 [19] Bai et al., 2022 [26] Lin et al., 2024 [27] Wang et al., 2022 [42]	IL-5 expression
Viksne et al., 2022 [28] Yu et al., 2022 [25]	IL-10 expression
Gao et al., 2024 [44] Viksne et al., 2022 [28]	IL-6 expression
Mohamed et al., 2023 [15] Peng et al., 2023 [24]	Prior sinus surgery
Abuduruk et al., 2024 [19] Bouatay et al., 2024 [18]	Compliance with post-procedure recommendations

Chen et al. [43] examined Charcot–Leyden crystals (CLCs) in nasal secretions and found elevated levels in 85% of recurrent CRSwNP cases, with high sensitivity and specificity for predicting postoperative recurrence. Gao et al. [44] demonstrated that higher serum immunoglobulin E (sIgE) and IL-6 levels, alongside lower regulatory T cell (Treg) percentages, were associated with recurrence in eosinophilic CRSwNP patients, with combined marker analysis yielding high predictive accuracy.

Finally, Moreno-Jimenez et al. [45] showed increased expression of thymic stromal lymphopoietin (TSLP) in nasal polyps and elevated TSLP receptor (TSLPR) expression in peripheral blood of CRSwNP patients with low eosinophilia, suggesting these molecules as minimally invasive biomarkers and potential therapeutic targets.

Table 2, **Table 3**, and **Table 4** summarize the results of the studies included in the review.

Discussion

Recurrence of nasal polyps after endoscopic sinus surgery remains a significant challenge in the management of chronic rhinosinusitis with nasal polyps. It is estimated that approximately 20% of CRSwNP patients experience polyp recurrence within 5 years following ESS [46]. The studies included in this review reported an average recurrence rate of 28%, based on follow-up periods ranging from 6 to 69 months. Notably, the highest risk of relapse occurs within the first postoperative year, highlighting the need for close monitoring during this critical period [15–45].

Multiple risk factors for polyp recurrence have been consistently identified. Comorbid asthma, allergic rhinitis, and aspirin-exacerbated respiratory disease (AERD) are strongly associated with higher relapse rates [15–20,24–28,36,42,44]. Systemic eosinophilia and elevated levels of inflammatory cytokines, particularly IL-5, IL-6, and IL-10, further contribute to persistent disease and polyp regrowth [15–20,24–28,36,42,47]. Patient-related factors, such as smoking, poor adherence to postoperative care protocols, and a history of previous sinus surgeries, have also been implicated in increasing the risk of recurrence [15–45]. **Table 5** lists the most common risk factors found.

Recent molecular studies have provided new insights into the pathophysiological mechanisms underlying polyp recurrence. Biomarkers related to inflammation (e.g., NOS2, RANTES, ALCAM, BAFF, CSF1R, sST2, S100A8, SERPINB10, B7-H4, miR-3174, miR-192-3p) and tissue remodeling (e.g., MMP-2, MMP-7, MMP-9, and their inhibitors TIMP-1, TIMP-2) show promise as predictors of postoperative outcomes [29–43]. Charcot–Leyden crystals have also emerged as potential indicators of recurrence due to their association with eosinophilic inflammation [43]. However, these findings remain preliminary and require validation in larger, prospective studies before they can be integrated into routine clinical practice.

Importantly, the inflammatory phenotype of CRSwNP appears to influence recurrence patterns. Patients with eosinophilic CRSwNP consistently exhibit higher relapse rates than those with non-eosinophilic forms [34,37,40,41,44]. In contrast, the role of neutrophilic infiltration is less well defined, with conflicting evidence regarding its contribution to polyp regrowth [23,25,44].

While these insights represent significant progress, heterogeneity across studies – particularly in terms of follow-up duration, patient population, and biomarker assessment – limits direct comparisons and underscores the need for standardized methodologies. Future research should prioritize large-scale, longitudinal studies to validate promising biomarkers and explore targeted therapeutic strategies.

In clinical practice, incorporating established risk factors and emerging molecular markers into pre- and postoperative assessments may facilitate more personalized management strategies, ultimately improving long-term disease control and reducing recurrence rates.

Conclusions

Based on the reviewed evidence, the recurrence of nasal polyps after endoscopic sinus surgery in patients with CRSwNP is a multifactorial process involving complex immune and inflammatory pathways. Numerous studies have identified elevated levels of type 2 cytokines, eosinophil-associated markers, matrix metalloproteinases, and immune regulatory molecules as key contributors to polyp relapse. Biomarkers such as ALCAM, Charcot–Leyden crystals, mucins, and combined assessments of sIgE, IL-6, and regulatory T-cells show significant potential in predicting postoperative recurrence.

These insights underscore the importance of integrating biomarker evaluation into clinical practice to better stratify a patient's risk of recurrence, enabling personalized postoperative management. Continued research is essential to further validate these biomarkers and to develop targeted therapeutic strategies aimed at reducing polyp recurrence and improving long-term outcomes for patients.

Ultimately, improving the prediction and prevention of polyp recurrence has the potential to significantly enhance the quality of life for affected patients by reducing symptoms, decreasing the need for repeated surgeries, and minimizing the burden of chronic inflammation.

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