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Biomarkers of Sinonasal Polyposis: Can Recurrence after Surgery be Predicted?

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Abstract | **Review Article**

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a heterogeneous inflammatory disease, predominantly of type 2, whose management relies on endoscopic surgery but is marked by frequent recurrence, with reported rates ranging from 4% to 60% depending on the series. Identifying patients at high risk of recurrence would make it possible to adapt postoperative treatment and surveillance. This narrative review takes stock of the biomarkers studied as predictors of recurrence after surgery, assesses their predictive value and limitations, and discusses their applicability in clinical practice. Tissue markers (tissue eosinophilia, Charcot-Leyden crystals/galectin-10, mast cells), markers in nasal secretions (IL-5, IgE, ECP), serum and blood markers (periostin, IL-33 and sST2, neutrophil-to-lymphocyte ratio, blood eosinophilia) and associated clinical factors (asthma, aspirin intolerance) were examined. Although the data converge towards a central role of type 2 inflammation, no single biomarker can currently predict recurrence reliably. Interpretation is limited by heterogeneous definitions of recurrence, population-dependent thresholds, non-standardized methods and small sample sizes. Combined approaches integrating clinical data with blood and tissue markers appear more promising than any single marker. Harmonized definitions and validation in prospective multicenter cohorts are needed before biomarkers can complement clinical factors in the personalized postoperative management of these patients.

Keywords: Chronic rhinosinusitis; Nasal polyps; Biomarkers; Recurrence; Type 2 inflammation; Tissue eosinophilia; Endoscopic sinus surgery.

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1. INTRODUCTION

Chronic rhinosinusitis (CRS) is a common inflammatory disease, affecting about 11% of the European population [1]. According to the EPOS 2020 guidelines, it is classified by clinical phenotype into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [1,2]. Sinonasal polyposis causes nasal obstruction, rhinorrhea, hyposmia or anosmia and facial pressure, and substantially impairs quality of life [3].

Management relies on maximal medical treatment and, when this fails, on endoscopic endonasal surgery. Surgery nevertheless carries a high risk of recurrence: more than half of patients relapse within three years of the procedure [1]. Reported rates vary widely, from 4% to 60% depending on the series [4], which partly reflects the lack of a consensus definition of recurrence (endoscopic or symptomatic recurrence, need for systemic corticosteroids or revision surgery) as well as variable follow-up durations.

In this context, identifying patients at high risk of recurrence before or at the time of surgery is a major challenge. It would make it possible to adjust the intensity of postoperative treatment, plan surveillance and refer patients earlier to biologic therapy. Although clinical factors such as asthma and aspirin intolerance are classically associated with recurrence, many clinical and immunological factors remain poorly understood [4]. The shift from a phenotypic classification to an endotype-based approach has renewed interest in tissue, blood and local biomarkers.

The aim of this narrative review is to take stock of the biomarkers studied as predictors of recurrence after surgery for sinonasal polyposis, to assess their predictive value and limitations, and to discuss their applicability in clinical practice.

2. Pathophysiology: from phenotypic classification to endotypes

CRSwNP is a heterogeneous inflammatory disease, predominantly of type 2 [1]. In Western populations, type 2 inflammation predominates in the majority of patients [5]. It classically involves cytokines such as IL-4, IL-5 and IL-13, local IgE production, and the recruitment and activation of eosinophils, resulting in the release of granule proteins such as ECP, EDN, MBP, EPX, and galectin-10, the component of Charcot-Leyden crystals [5]. The latter are associated with eosinophil activation and cytolysis as well as with extracellular trap cell death (EETosis) [5].

This heterogeneity varies across populations. In Japan, for example, CRSwNP is usually divided into eosinophilic CRS (ECRS) and non-eosinophilic CRS, based on the JESREC score and the number of tissue eosinophils [6]. Non-type 2 endotypes (neutrophilic, Th1/Th17 profiles), more frequent in some Asian populations, are less well characterized. This diversity partly explains why thresholds and biomarkers validated in one population cannot always be transposed to another, a point we discuss in the remainder of this work.

3. Biomarkers studied as predictors of recurrence

3.1. Tissue biomarkers

Tissue eosinophilia.

This is the most studied marker. A meta-analysis of 11 studies (n = 3183) recommends a threshold above 55 eosinophils per high-power field to predict recurrence, with no demonstrated effect of geographic location, follow-up duration or study design on test performance [7]. This conclusion is not unanimous, however: a recent Spanish study of a Western cohort of 54 operated patients found no association between tissue eosinophil count and recurrence [3]. A critical analysis of this work points out the limitations of measures based on a single cell type, without calling into question the value of tissue analysis [8].

Charcot-Leyden crystals (galectin-10).

In a cohort of 110 patients followed for 24 months, 30% had polyp recurrence, and the number of tissue crystals was associated with recurrence in multivariate analysis (adjusted OR of about 2.1) [9]. Protein and mRNA levels of galectin-10 in nasal secretions and nasal brushings have also been associated with recurrence [9]. Their detection remains delicate, however: depending on the cutting angle, the needle-shaped structures can be hard to identify, and revealing them by immunofluorescence is long and laborious [10].

Other tissue markers.

A model combining tissue biomarkers and clinical variables associated ECP, IL-5 and anti-double-stranded DNA IgG with asthma and the preoperative CT score to predict recurrence with good accuracy [11]. In a Japanese study of 32 patients, mast cell counts in resected polyps are proposed as a complementary approach to predict recurrence [6], but the sample is small and these results need to be confirmed.

3.2. Markers in nasal secretions

A simple approach based on nasal secretion sampling was evaluated in a cohort of 48 patients from Lille: IL-5, IgE and ECP levels were significantly higher in patients requiring revision surgery, pointing to a profile dominated by type 2 proteins [12].

3.3. Serum and blood markers

Periostin.

In a Japanese study based on the JESREC classification, postoperative recurrence differed significantly between the high and low serum periostin groups, with a threshold set at 115.5 ng/ml ($p = 0.0072$) [13]. A more recent study finds that preoperative serum periostin, eotaxin-3 and procalcitonin are correlated with postoperative severity and recurrence, notably with POSE scores at 1 and 3 years [1].

IL-33 and sST2.

Serum IL-33 and sST2 levels are higher in patients than in controls, especially in the eosinophilic form, and their combination improves the accuracy of recurrence prediction compared with each marker alone [14].

Neutrophil-to-lymphocyte ratio (NLR).

It is an independent risk factor for recurrence in a retrospective study of 192 patients, with the advantage of being calculable from a simple complete blood count, but it should be interpreted with caution given the retrospective design [15].

Blood eosinophilia.

Results are discordant. In the Spanish study cited above, blood eosinophilia was related to disease severity and control, unlike the tissue count [3]. In the cohort studying Charcot-Leyden crystals, the number and percentage of circulating eosinophils were higher in the recurrence group [9]. Note that a meta-analysis concludes that the evidence is insufficient to make it a good predictor of ECRS [16].

3.4. Associated clinical factors

Asthma and aspirin intolerance are more frequent in patients who relapse in the long term, whereas atopy did not differ significantly between groups [4]. In the Charcot-Leyden crystal cohort, male sex and asthma were also among the predictors of recurrence [9].

4. Predictive value of biomarkers: critical synthesis

4.1. A heterogeneously defined recurrence

Comparison of studies is first hampered by the absence of a common definition of the event to be predicted. Depending on the study, recurrence

corresponds to the need for revision surgery (16.7% in the Lille cohort) [12], to the need for maximal medical treatment or revision surgery (40% at 8-10 years) [4], or to the reappearance of polyps at 24 months (30%) [9]. The Spanish study reports 43.5% recurrence among operated patients [3]. Follow-up durations range from 2 to 10 years. A predictive value therefore only makes sense when related to a specific definition and time horizon.

4.2. Thresholds and populations

The tissue eosinophil threshold of 55 per field was first established in an Asian population [3], then supported by the meta-analysis, which finds no effect of geographic area on test accuracy [7]. It was nevertheless not reproduced in the Spanish cohort [3]. Similarly, the serum periostin threshold of 115.5 ng/ml comes from a Japanese study using the JESREC classification [13], and its transposition to other populations remains to be demonstrated. The weight of non-type 2 endotypes (more frequent in some Asian populations) could explain part of these discrepancies.

4.3. Methodological limitations

- **Small samples**: 32 patients for mast cells [6], 48 for nasal secretions [12], 54 for the Spanish study [3].
- **Designs**: NLR relies on a retrospective review [15], with its usual biases.
- **Lack of standardization**: detection of Charcot-Leyden crystals depends on the method (standard staining or immunofluorescence) and on the cutting angle [10], and serum assays vary with ELISA kits and the thresholds used.
- **Lack of a common framework**: a recent commentary calls for a consensus framework cross-referencing clinical classifications, EPOS control criteria and biological variables (blood eosinophils, total IgE, periostin) to allow meta-analyses [8].

4.4. Towards combined approaches

No single marker achieves consensus, but combined approaches give encouraging results: the association of tissue biomarkers (ECP, IL-5, anti-double-stranded DNA IgG) and clinical variables (asthma, preoperative CT score) predicts recurrence with good accuracy [11], and the combination of IL-33 and sST2 outperforms each marker alone [14]. These results suggest that a multiparametric model combining clinical data, accessible blood markers and tissue markers is more realistic than a single biomarker.

Summary table

Biomarker	Sample	Main finding	Main limitation
Tissue eosinophilia	Biopsy / surgical specimen	Threshold >55/field recommended by a meta-analysis of 11 studies (n = 3183) [7]	Not found in a Spanish cohort (n = 54) [3]
Charcot-Leyden crystals	Tissue, secretions, brushing	Adjusted OR ≈ 2.1 (n = 110, 24-month follow-up) [9]	Non-standardized detection [10]
Mast cells	Surgical specimen	Complementary lead in ECRS [6]	n = 32
IL-5, IgE, ECP	Nasal secretions	Higher levels if revision surgery [12]	n = 48, 8 revisions
Periostin	Serum	Recurrence differs according to a 115.5 ng/ml threshold [13]	Japanese study, threshold not validated elsewhere
IL-33 and sST2	Serum	Better accuracy in combination [14]	No established clinical threshold
NLR	Blood (CBC)	Independent risk factor (n = 192) [15]	Retrospective study
Blood eosinophilia	Blood (CBC)	Discordant results across studies [3,9]	No consensus threshold
Asthma, aspirin intolerance	Clinical	More frequent in long-term recurrences [4]	Risk factors, not biomarkers in the strict sense

5. Practical implications

5.1. Which markers can be used in routine practice?

Applicability varies greatly from one marker to another. Parameters derived from the complete blood count (blood eosinophilia, NLR) and from standard pathological examination (tissue eosinophils, for which a threshold of 10 per high-power field defines tissue eosinophilia according to EPOS 2020 [2]) can be obtained in most centers. Conversely, detection of Charcot-Leyden crystals by immunofluorescence and ELISA assays of periostin, IL-33, sST2 or ECP remain in the research domain, without a validated threshold. This assessment of feasibility reflects our own analysis and depends on local technical facilities.

5.2. Adapting postoperative treatment

Identifying a high-risk profile (marked type 2 inflammation, associated asthma, aspirin intolerance) should in principle justify closer endoscopic surveillance and optimization of local postoperative treatment. To our knowledge, no study retained in this review validates a postoperative corticosteroid strategy adapted to a biomarker: this point, important in practice, remains to be explored.

5.3. Role of biologics and link with biomarkers

The 2023 EPOS/EUFOREA update defines the indications for biologics from type 2 inflammation markers: tissue eosinophils ≥ 10 per field, blood eosinophils ≥ 150, or total IgE ≥ 100, the blood threshold having been lowered from 250 to 150 cells/µL [17,18]. This criterion is added to four others (need for systemic corticosteroids, SNOT-22 ≥ 40, anosmia, associated asthma), three of the five criteria being required [17], in patients with bilateral polyps after endoscopic surgery [18]. The experts discussed making type 2 inflammation mandatory, but this proposal was not retained because of definitions that are still imprecise [17]. Response to treatment is assessed on five criteria, with a first evaluation at 6 months [18].

One point deserves emphasis in the discussion: the markers that define eligibility for biologics (eosinophils, IgE) are the very ones studied as predictors of recurrence. In practice, patients at high risk of recurrence are largely those likely to meet the indication criteria, but these criteria were not designed to predict recurrence after surgery, and their own prognostic value remains to be established. Moreover, these criteria remain restrictive in practice: in a post hoc analysis of phase 3 trials, only 55% of included patients met the EUFOREA/EPOS criteria for biologic eligibility [19].

Finally, the combination of surgery and biologic therapy is attracting growing interest: in a retrospective cohort, adding postoperative dupilumab was associated with a greater reduction in polyp and endoscopic scores compared with surgery alone [20]. These retrospective data should be considered exploratory.

6. Perspectives and conclusion

6.1. Perspectives

Several avenues emerge to make recurrence prediction more reliable and applicable.

Harmonize definitions and protocols.

A consensus definition of recurrence (endoscopic, symptomatic, need for systemic corticosteroids or revision surgery) and a standardized follow-up horizon are a prerequisite for any comparison between studies. The same applies to the method of measuring markers: a recent commentary advocates a consensus framework cross-referencing clinical classifications, EPOS control criteria and biological variables to allow meta-analyses [8].

Validate thresholds in prospective multicenter cohorts.

The proposed thresholds (tissue eosinophils, serum periostin) often come from single-center studies or from a given population, and have not been consistently confirmed in other settings. Prospective cohorts including diverse populations are needed.

Develop combined models.

The most encouraging results come from combining several parameters: tissue biomarkers and clinical variables on the one hand [11], serum IL-33 and sST2 on the other [14]. The next step would be to build and validate prognostic scores integrating clinical data, accessible blood markers and, where available, tissue markers.

Favor minimally invasive sampling.

Nasal secretions and blood offer an alternative to biopsy for follow-up, provided that collection and assay techniques are standardized.

Link recurrence prediction and indication for biologics.

Experts stress that it is crucial to acquire real-life data and information on measuring type 2 inflammation at a reasonable cost [17]. Assessing whether the eligibility criteria for biologics also have prognostic value after surgery would help identify patients who would benefit from early management.

6.2. CONCLUSION

To answer the question posed in the title: to date, it is not possible to reliably predict recurrence of sinonasal polyposis after surgery from a single biomarker. The data converge towards a central role for type 2 inflammation, with repeated associations between recurrence and tissue eosinophilia, Charcot-Leyden crystals, periostin, IL-5 and ECP, as well as clinical factors such as asthma and aspirin intolerance. But the heterogeneity of definitions, thresholds, populations and methods, together with the often-small sample sizes, limits the reach of these results and their transposition into clinical practice.

In the current state of knowledge, biomarkers should be considered a complement to clinical factors, not a substitute. Combined approaches, validated in prospective multicenter cohorts, are the most promising route to personalized management of these patients.

REFERENCES

1. Florean MD, Mare C, Gâta A, Trombitaș VE, Budișan L, Zanoaga O, *et al.,* Serum biomarkers as predictors of recurrence in chronic rhinosinusitis with nasal polyps. Medicina (Kaunas). 2026;62(8):1452. doi:10.3390/medicina62081452
2. Fokkens WJ, Lund VJ, Hopkins C, *et al.,*European position paper on rhinosinusitis and nasal polyps 2020. Rhinology. 2020;58(Suppl S29):1-464. doi:10.4193/Rhin20.600
3. Vizcarra-Melgar J, Sánchez-Gómez S, López-González N, Moreno-Luna R, González-García J, Maza-Solano J. Tissue eosinophil level as a predictor of control, severity, and recurrence of chronic rhinosinusitis with nasal polyps. Front

Allergy. 2025; 6:1549332. doi:10.3389/falgy.2025.1549332

4. Rosati D, Rosato C, Pagliuca G, *et al.,* Predictive markers of long-term recurrence in chronic rhinosinusitis with nasal polyps. Am J Otolaryngol. 2020;41(1):102286. doi: 10.1016/j.amjoto.2019.102286
5. Kamiński B, Ochab D, Kopczyński J, Łacwik P, Pałczyński C. Galectin-10 and Charcot-Leyden crystals in chronic rhinosinusitis with nasal polyps: pathogenetic insights and clinical implications. Diagnostics (Basel). 2026;16(17):2737. doi:10.3390/diagnostics16172737
6. Teranishi Y, Jin D, Takano S, Sunami K, Takai S. Decrease in number of mast cells in resected nasal polyps as an indicator for postoperative recurrence of chronic rhinosinusitis. Immun Inflamm Dis. 2019;7(3):191-200. doi:10.1002/iid3.261
7. McHugh T, Snidvongs K, Xie M, Banglawala S, Sommer D. High tissue eosinophilia as a marker to predict recurrence for eosinophilic chronic rhinosinusitis: a systematic review and meta-analysis. Int Forum Allergy Rhinol. 2018;8(12):1421-1429. doi:10.1002/alr.22194
8. Gelardi M. Commentary: Tissue eosinophil level as a predictor of control, severity, and recurrence of chronic rhinosinusitis with nasal polyps. Front Allergy. 2025;6:1628864. doi:10.3389/falgy.2025.1628864
9. Chen W, Bai Y, Kong W, *et al.,* Predictive significance of Charcot-Leyden crystal structures for nasal polyp recurrence. Clin Transl Allergy. 2022;12(11):e12212. doi:10.1002/clt2.12212
10. Sasaki T, Suzaki I, Ueki S. Charcot-Leyden crystals in tissues. Clin Transl Allergy. 2023;13(7):e12275. doi:10.1002/clt2.12275
11. Bai J, Huang JH, Price CPE, *et al.,* Prognostic factors for polyp recurrence in chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol. 2022;150(2):352-361.e7. doi:10.1016/j.jaci.2022.02.029
12. Mortuaire G, Gengler I, Carpentier C, Szymanski C, Chenivesse C, Lefevre G. T helper 2 inflammatory markers are associated with recurrence in chronic rhinosinusitis with nasal polyps after endoscopic sinus surgery. Rhinology. 2020;58(5):444-450.
13. Ninomiya T, Noguchi E, Haruna T, Hasegawa M, Yoshida T, Yamashita Y, *et al.,* Periostin as a novel biomarker for postoperative recurrence of chronic rhinosinusitis with nasal polyps. Sci Rep. 2018;8:11450. doi:10.1038/s41598-018-29612-2
14. Zhang Y, Zhu K, Chen J, Xia C, Yu C, Gao T, *et al.,* Predictive values of serum IL-33 and sST2 in endotypes and postoperative recurrence of chronic rhinosinusitis with nasal polyps. Mediators Inflamm. 2022;2022:9155080. doi:10.1155/2022/9155080
15. Boztepe OF, Gün T, Demir M, Gür ÖE, Ozel D, Doğru H. A novel predictive marker for the recurrence of nasal polyposis following endoscopic sinus surgery. Eur Arch Otorhinolaryngol. 2016;273(6):1439-1444. doi:10.1007/s00405-015-3753-z
16. Yin X, Chang D, Sun C. Predictive value of peripheral blood eosinophil levels for eosinophilic chronic rhinosinusitis: a systematic review and meta-analysis. J Laryngol Otol. 2025;139(2):95-101. doi:10.1017/S0022215124001208
17. Fokkens WJ, Viskens AS, Backer V, Conti D, De Corso E, Gevaert P, *et al.,* EPOS/EUFOREA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. Rhinology. 2023;61(3):194-202. doi:10.4193/Rhin22.489
18. Lee KI, Ryu G, Yoo SH, Cho HJ, Mo JH, Kim CH; Korean Rhinologic Society. Biologics for chronic rhinosinusitis with nasal polyps: current status and clinical considerations in Korea. J Rhinol. 2025;32(1):1-9. doi:10.18787/jr.2025.00002
19. EUFOREA/EPOS criteria applied to a diverse CRSwNP cohort: post hoc findings from twice-yearly depemokimab ANCHOR-1/-2 trials. Poster D2.450, EAACI Congress.
20. Liu CN, Yeh TH, Lin CF, Lin YT. The efficacy of dupilumab as an adjuvant treatment after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps: a retrospective cohort analysis. Clin Exp Otorhinolaryngol. 2025;18:271-279. doi:10.21053/ceo.2024.00310