Am J Transl Res 2024;16(12):7609-7617
www.ajtr.org /ISSN:1943-8141/AJTR0161374

Original Article

Risk factors for postoperative relapse of chronic rhinosinusitis with nasal polyps and improvement in clinical treatment

Wuchen Wang[1*], Junmei Fu[1*], Wenshuai Chang[2]

[1]*Department of Otolaryngology, The First People's Hospital of Jiangxia District, Wuhan 430200, Hubei, China;* [2]*Department of Otolaryngology, Air Force Hospital of The Central Theater Command of PLA, Datong 037006, Shanxi, China.* [*]*Equal contributors and co-first authors.*

Received October 22, 2024; Accepted December 4, 2024; Epub December 15, 2024; Published December 30, 2024

Abstract: Objectives: To identify the risk factors for postoperative relapse of chronic rhinosinusitis with nasal polyps (CRSwNP) using multivariate Logistic regression analysis and to explore potential improvements in clinical treatment measures. Methods: We selected 270 CRSwNP patients who underwent surgery at The First People's Hospital of Jiangxia District between January 2022 and July 2024. The patients were divided into two groups based on the presence or absence of postoperative relapse: 40 cases with relapse were designated as the relapse group, and the other 230 cases without relapse were designated as the non-relapse group. Serum samples were collected from both groups before surgery to measure eosinophilic cationic protein (ECP)/myeloperoxidase (MPO), immunoglobulin E (IgE), and C-C motif chemokine ligand 4 (CCL4). Receiver operating characteristic (ROC) curves were used to analyze the predictive value of these indices for postoperative relapse in CRSwNP patients. The correlation of these indices with postoperative relapse was analyzed using Spearman's correlation coefficients. Univariate and multivariate analyses were employed to identify factors influencing postoperative relapse of CRSwNP. Results: The relapse group showed markedly higher ECP/MPO, IgE, and CCL4 compared to the non-relapse group. The area under the curve (AUC) for predicting postoperative relapse of CRSwNP by each single indicator approximated 0.800, while the AUC of combined detection was above 0.900. ECP/MPO, IgE, and CCL4 all exhibited a significant positive correlation with postoperative relapse of CRSwNP. Univariate analysis revealed that the postoperative relapse of CRSwNP was significantly linked to the Davos score of nasal polyps, smoking history, postoperative infection, ECP/MPO, IgE, and CCL4. Multivariate analysis confirmed that ECP/MPO, IgE, and CCL4 were independent risk factors for postoperative recurrence of CRSwNP. Conclusions: ECP/MPO, IgE, and CCL4 are reliable predictors of postoperative relapse in CRSwNP patients, and their combined detection can further enhance the predictive accuracy. These biomarkers are closely and positively correlated with postoperative relapse and serve as risk factors for postoperative recurrence. Given the elevated risk of postoperative recurrence in CRSwNP patients with high levels of ECP/MPO, IgE, and CCL4, it is recommended to optimize clinical treatment strategies for these patients to reduce the likelihood of recurrence.

Keywords: Chronic rhinosinusitis, nasal polyps, postoperative relapse, multivariate Logistic regression analysis, improvement in clinical treatment

Introduction

Chronic rhinosinusitis (CRS) is an upper airway inflammatory disorder primarily affecting the nasal cavity and sinus mucosa. It is not only prevalent but also characterized by a complex pathological process and diverse etiology [1, 2]. Generally, CRS is classified into two types based on the presence or absence of nasal polyps, namely CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [3]. In comparison to the latter, CRSwNP has a higher incidence risk, with patients typically experiencing more severe clinical manifestations, greater impairment to their quality of life, and a heavier personal and socioeconomic burden [4, 5]. CRSwNP patients often present with several comorbidities, such as asthma, sleep disorders, allergic rhinitis, gastroesophageal reflux disease, and cognitive dysfunction, which affect their daily lives to varying degrees [6]. Epidemiological data indicate that CRSwNP

https://doi.org/10.62347/CHQV3614

affects 0.5-4.0% of the global population [7]. Currently, surgical intervention is the main treatment modality for CRSwNP. However, there is a certain risk of postoperative recurrence, which increases the complexity of treatment [8]. To alleviate the disease impact and reduce the economic burden on CRSwNP patients, it is crucial for healthcare providers to explore the risk factors for postoperative relapse and optimize the treatment and management strategies for CRSwNP.

Eosinophilic cationic protein (ECP), a biomarker derived from eosinophil secretory granules, is released in response to stimuli such as immunoglobulins and complements. It exhibits antibacterial and antiviral properties and has been identified as a potential marker of eosinophilic inflammation [9, 10]. Myeloperoxidase (MPO), essentially a heme enzyme, can be used for screening infectious rhinitis [11]. ECP/MPO levels can also serve as an indicator for the endotype diagnosis of CRS [12]. Previous research has also indicated that immunoglobulin E (IgE), closely associated with elevated eosinophilic inflammation, plays a significant role in the pathophysiological process of nasal polyposis to some extent [13]. C-C motif chemokine ligand 4 (CCL4), a CC chemokine related to immune cell transport and derived from airway epithelial cells, influences the accumulation and activation of eosinophils at inflammatory sites [14, 15]. Despite their potential relevance, limited studies have investigated whether ECP/MPO, IgE, and CCL4 can predict postoperative relapse of CRSwNP and serve as risk factors for recurrence. This study aims to address this gap by analyzing these biomarkers to contribute to the prevention of postoperative recurrence of CRSwNP.

Information and methodology

General information

This retrospective study was approved by the Ethics Committee of The First People's Hospital of Jiangxia District. This study selected 270 patients with CRSwNP who underwent surgical treatment at The First People's Hospital of Jiangxia District from January 2022 to July 2024. Of these, 40 cases were assigned to the relapse group and 230 to the non-relapse group. The two cohorts were clinically comparable, with no statistical difference in general information (P>0.05).

Inclusion and exclusion criteria

Inclusion criteria: Patients aged 18 years or older who met the diagnostic criteria for CRSwNP [16] and the Davos scoring criteria for nasal polyps [17]; All patients were treatment-naive, diagnosed at our hospital, and underwent endoscopic sinus surgery; no relevant drug treatment in the four weeks prior to operation; no history of postoperative medication; and intact clinical data and case records.

Exclusion criteria: Those with fungal sinusitis, posterior maxillary sinus nostril polyps, a history of endoscopic sinus surgery, impaired heart, lung, or kidney function, infectious diseases, or immune system disorders; pregnant or lactating women.

Treatment

Preoperative nasal endoscopy and coronal CT scans of the sinuses were carried out. Under general anesthesia, the operation was completed using the Messerklinger technique. The procedure involved the removal of nasal polyps, resection of the uncinate process, and opening of the sphenoid, ethmoid, or frontal sinuses. The maxillary sinus ostium was enlarged, and the diseased tissues in the sinus cavity and ostium were removed. Both groups received routine anti-infection treatment after the operation.

Detection indicators

Fasting venous blood (2 mL) was collected from all patients in the morning, and the serum was separated by centrifugation. Biochemical indexes, including ECP and MPO levels, were detected by enzyme-linked immunosorbent assay (ELISA), and the ECP/MPO ratio was calculated. Serum IgE levels were quantified using radioimmunoassay, and CCL4 levels were detected by liquid-phase chip technology.

Patients' medical records were retrieved from the hospital's electronic medical record system. Information such as age, gender, body mass index (BMI), the course of chronic sinusitis, Davos score of nasal polyps, lesion location, smoking history, alcohol consumption his-

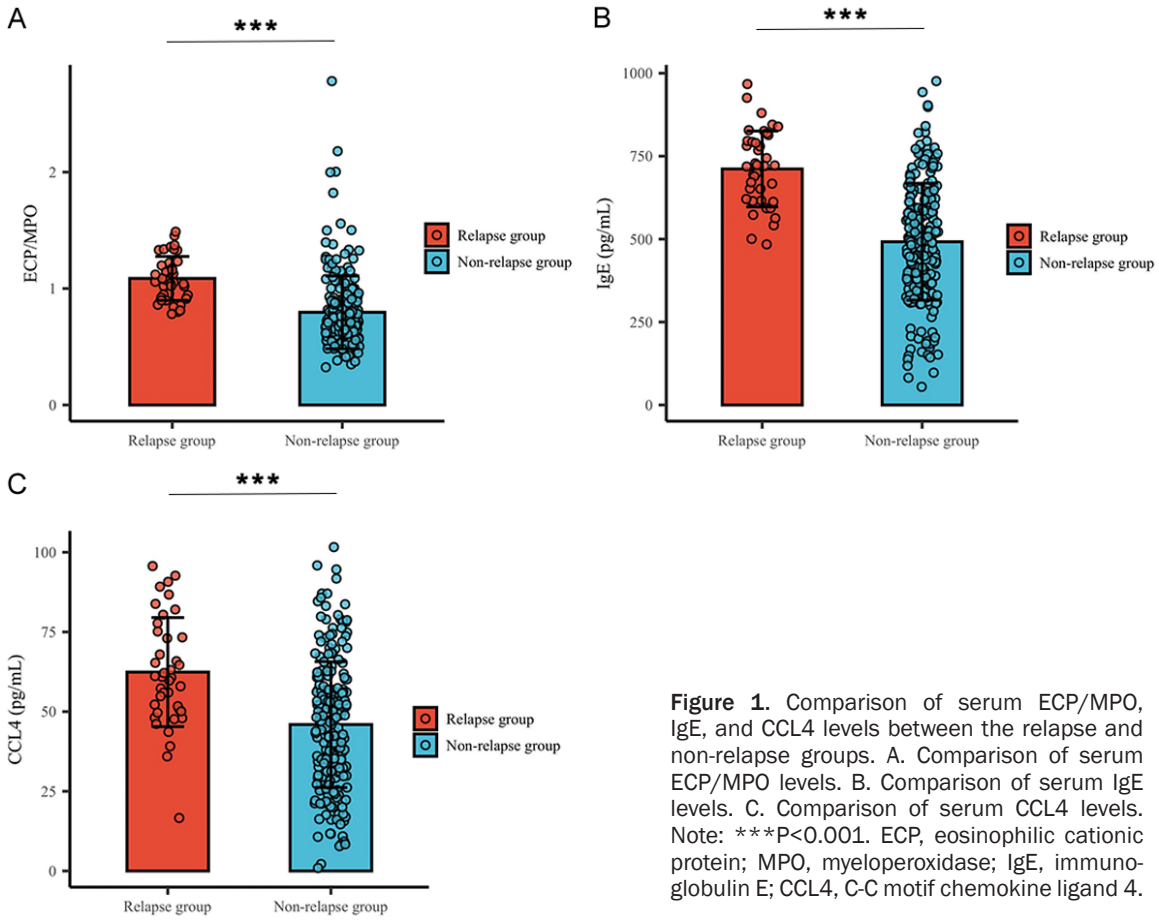

Figure 1. Comparison of serum ECP/MPO, IgE, and CCL4 levels between the relapse and non-relapse groups. A. Comparison of serum ECP/MPO levels. B. Comparison of serum IgE levels. C. Comparison of serum CCL4 levels. Note: ***P<0.001. ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4.

tory, and postoperative infections was collected. The relationship between the above-mentioned indicators and postoperative relapse was analyzed through univariate and multivariate analyses.

Statistical analysis

SPSS 21.0 was used for data analysis. For continuous data, mean ± standard error of the mean (SEM) was used for statistical description; the independent samples t-test was used for comparison between the two groups, and the paired t-test was used for comparison before and after treatment. For count data, rate (percentage) was used for representation, and the χ^2 test was employed for comparison between groups. The estimation of the sample size in this study was based on the empirical rule of multivariate Logistic regression analysis. That is, the sample size should be at least 10 to 15 times the number of covariates. Assuming 10 covariates, the required sample size was calculated to be between 100 and 150 cases. The inclusion of 270 patients in this study far exceeded the minimum requirement, ensuring sufficient statistical power for the analysis. A *P*-value less than 0.05 indicated a statistically significant difference.

Results

Comparison of serum ECP/MPO, IgE, and CCL4 levels between the relapse and non-relapse groups

The serum levels of ECP/MPO, IgE, and CCL4 in the relapse group were (1.09±0.19), (711.42±114.22) pg/mL, and (62.40±17.12) pg/mL, respectively, compared to (0.80±0.31), (492.05±176.16) pg/mL, and (45.93±19.75) pg/mL in the non-relapse group (all P<0.001; **Figure 1**; **Table 1**).

Prediction of postoperative relapse of CRSwNP

ROC analysis was conducted to evaluate the predictive value of serum ECP/MPO, IgE, and

Table 1. Comparison of serum ECP/MPO, IgE, and CCL4 levels between the relapse and non-relapse groups

Indicators	Relapse group (n=40)	Non-relapse group (n=230)	χ^2/t	P
ECP/MPO	1.09±0.19	0.80±0.31	5.727	<0.001
IgE (pg/mL)	711.42±114.22	492.05±176.16	7.597	<0.001
CCL4 (pg/mL)	62.40±17.12	45.93±19.75	4.958	<0.001

Note: ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4.

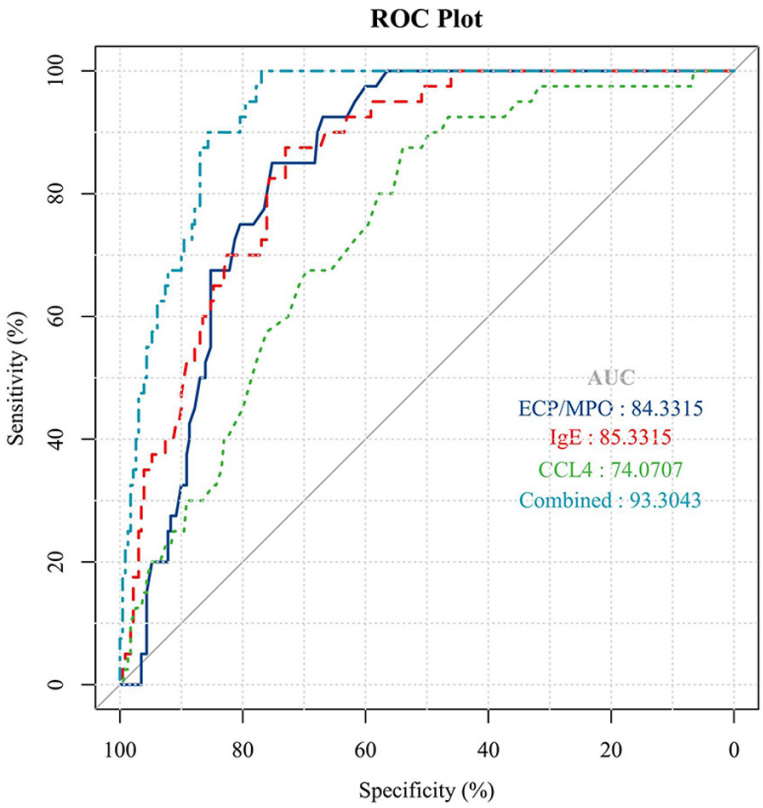

Figure 2. ROC analysis of the predictive value of ECP/MPO, IgE, and CCL4 for postoperative relapse of CRSwNP. ROC, receiver operating characteristic; ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4; CRSwNP, chronic rhinosinusitis with nasal polyps.

CCL4 for postoperative relapse of CRSwNP. The analysis results indicated that the area under the curve (AUC) for ECP/MPO predicting postoperative relapse of CRSwNP was 0.843, with specificity and sensitivity being 85.00% and 75.22%, respectively, and the optimal cut-off value being 0.90. The AUC of IgE for predicting postoperative recurrence of CRSwNP was 0.853, with the specificity, sensitivity, and optimal cut-off value being 87.50%, 73.04%, and 592.00 pg/mL, respectively. The AUC of CCL4 for predicting postoperative relapse of CRSwNP was 0.741, the specificity was 87.50%, the sensitivity was 53.91%, and the best cut-off value was 47.50 pg/mL. Furthermore, the combined AUC for predicting postoperative relapse using all three indicators was 0.933, with 100.00% specificity, 76.96% sensitivity, and an optimal cut-off value of 0.91 (**Figure 2** and **Table 2**).

Univariate analysis of factors influencing postoperative relapse of CRSwNP

Univariate analysis (**Table 3**) revealed significant associations between postoperative relapse of CRSwNP and the following factors: Davos score for nasal polyps, smoking history, and postoperative infection (all P<0.05). No significant associations were found with age, gender, BMI, course of chronic sinusitis, lesion location, or alcohol consumption history (all P>0.05).

Multivariate analysis of factors affecting postoperative relapse of CRSwNP

Variables with significant differences in the univariate analysis, as well as serum indicators such as ECP/MPO, IgE, and CCL4 with significant differences between groups, were taken as independent variables, and postoperative relapse was taken as the dependent variable (**Table 4**).

Multivariate binary Logistic regression analysis demonstrated that the Davos score for nasal polyps, postoperative infection, ECP/MPO, IgE, and CCL4 were all significant risk factors for postoperative relapse of CRSwNP (all P<0.05).

Table 2. Predictive performances of ECP/MPO, IgE, and CCL4 for postoperative relapse of CRSwNP analyzed by ROC curve analysis

Indicators	AUC	SE	*P* value	Specificity	Sensitivity	Optimal cutoff
ECP/MPO	0.843	0.025	<0.001	85.00%	75.22%	0.90
IgE	0.853	0.026	<0.001	87.50%	73.04%	592.00 pg/mL
CCL4	0.741	0.038	<0.001	87.50%	53.91%	47.50 pg/mL
Combined detection	0.933	0.015	<0.001	100.00%	76.96%	0.91

Note: ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4; CRSwNP, chronic rhinosinusitis with nasal polyps; ROC, receiver operation characteristics.

Table 3. Univariate analysis of factors influencing postoperative relapse of CRSwNP

Variable	Relapse group (n=40)	Non-relapse group (n=230)	χ^2/t	P
Age (years old)	40.70±9.41	41.83±12.03	0.565	0.573
Gender			0.316	0.574
Male	24 (60.00)	127 (55.22)		
Female	16 (40.00)	103 (44.78)		
Body mass index (kg/m^2)	23.32±2.48	23.50±2.44	0.430	0.668
Course of Chronic Sinusitis (Year)	5.78±2.06	5.57±2.14	0.576	0.565
Davos score of nasal polyps (points)	2.15±0.70	1.46±0.57	6.819	<0.001
Lesion location			2.020	0.155
Olfactory cleft polyp	12 (30.00)	46 (20.00)		
Nasal septum deviation	28 (70.00)	184 (80.00)		
Smoking history			6.251	0.012
Without	27 (67.50)	106 (46.09)		
With	13 (32.50)	124 (53.91)		
Alcoholism history			0.702	0.402
Without	18 (45.00)	120 (52.17)		
With	22 (55.00)	110 (47.83)		
Postoperative infection			9.150	0.003
Without	16 (40.00)	150 (65.22)		
With	24 (60.00)	80 (34.78)		

Note: CRSwNP, chronic rhinosinusitis with nasal polyps.

Table 4. Assignment table

Indicators	Variable	Quantization assignment
Davos score of nasal polyps	X1	<1.50 points =0, ≥1.50 points =1
Smoking history	X2	Without =0, with =1
Postoperative infection	X3	Without =0, with =1
ECP/MPO	X4	<0.90 =0, ≥0.90=1
IgE	X5	<592.00 pg/mL =0, ≥592.00 pg/mL =1
CCL4	X6	<47.50 pg/mL =0, ≥47.50 pg/mL =1
Postoperative relapse	Y	Non-relapse =0, relapse =1

Note: ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4.

However, smoking history was not found to be a significant risk factor (P>0.05; **Table 5**). Subsequently, a nomogram for predicting the postoperative relapse risk of CRSwNP was constructed based on the binary Logistic regression analysis. The total score ranged from 0 to

Table 5. Multivariate analysis of factors influencing postoperative relapse of CRSwNP

Variable	β	S.E.	Wald	P	OR	95% CI
Davos score of nasal polyps	1.849	0.552	11.197	0.001	6.352	2.151-18.756
Smoking history	-0.838	0.503	2.777	0.096	0.433	0.161-1.159
Postoperative infection	1.144	0.497	5.294	0.021	3.139	1.185-8.317
ECP/MPO	1.987	0.536	13.749	<0.001	7.293	2.551-20.847
IgE	1.761	0.576	9.355	0.002	5.821	1.883-17.997
CCL4	1.994	0.598	11.139	0.001	7.346	2.277-23.697

Note: ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4; CRSwNP, chronic rhinosinusitis with nasal polyps.

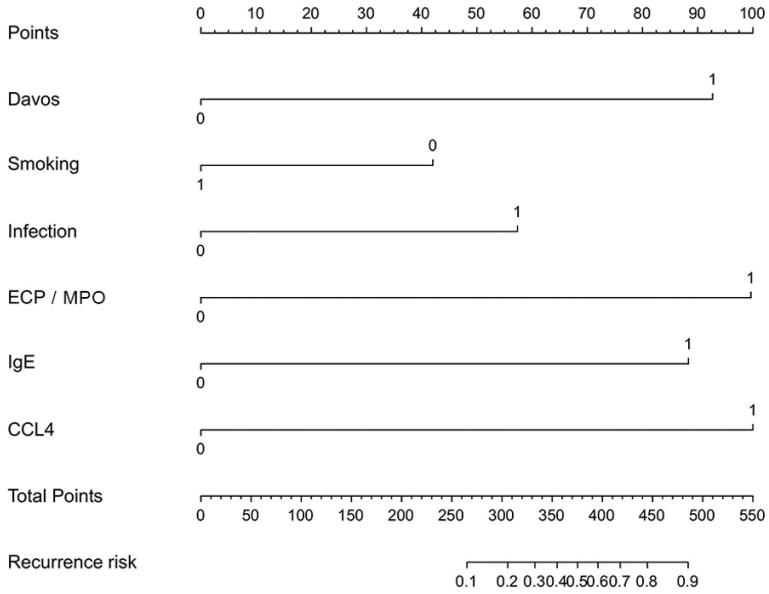

Figure 3. Nomogram for postoperative relapse risk of CRSwNP. ECP, eosinophilic cationic protein; MPO, myeloperoxidase; IgE, immunoglobulin E; CCL4, C-C motif chemokine ligand 4; CRSwNP, chronic rhinosinusitis with nasal polyps.

550 points, allowing prediction of the postoperative recurrence risk of CRSwNP within a range of 10.00%-90.00% (**Figure 3**).

Discussion

CRSsNP is an inflammatory infectious disease that can affect the frontal, sphenoid, ethmoid, and maxillary sinuses, causing symptoms such as facial pressure, a sense of fullness, dryness, dry cough, nasal congestion, and obstruction; in more severe cases, it may even lead to olfactory dysfunction and nasal mucosal congestion [18]. The development of this disease is influenced by multiple factors, including mucosal inflammation, environmental factors, and asthma history [19]. This study primarily focuses on analyzing the predictive value of ECP/MPO, IgE, and CCL4 in postoperative relapse of CRSwNP, identifying risk factors for postoperative recurrence, and proposing strategies to optimize clinical treatment.

Our study found that serum ECP/MPO, IgE, and CCL4 levels were abnormally elevated in the relapse group compared to the non-relapse group, suggesting that these markers may play a role in the pathological progression of CRSwNP and contribute to the postoperative recurrence of CRSwNP. This aligns with the findings of Van Zele T et al. [20], who observed higher levels of IgE and ECP in patients with recurrent CRSwNP.

ROC analysis revealed that the AUCs of serum ECP/MPO, IgE, and CCL4 for predicting postoperative relapse of CRSwNP were 0.843, 0.853, and 0.741, respectively. Among them, IgE exhibited the best predictive performance, followed by ECP/MPO and CCL4. Furthermore, the combined detection of these three factors for predicting the postoperative recurrence of CRSwNP showed an increased AUC to 0.933, with 100.00% specificity and 76.96% sensitivity. In the report by Zheng M et al. [21], the relapse group showed notably higher levels of ECP/MPO, IgE, and CCL4 than the non-relapse group; moreover, IgE demonstrated the highest sensitivity (82.4%) in predicting CRSwNP recurrence, and ECP/MPO presented the highest specificity (83.7%), which were similar to the findings of this study.

Univariate analysis identified several factors potentially linked to postoperative relapse, including Davos score of nasal polyps, smoking history, and postoperative infection. The Davos score, which reflects the severity of nasal polyps, was associated with an increased risk of recurrence. A higher Davos score may imply more severe nasal polyps, which could increase the risk of relapse after surgery [22]. Smoking, which harms the nasal mucosal defense mechanisms, exacerbates the inflammatory response and increases the risk of recurrence [23]. Postoperative infections, by triggering excessive inflammation and increased secretion in the nasal mucosa, can also contribute to higher relapse rates [24, 25]. Similarly, Fageeh YA et al. [26] indicated that smoking history, bilateral polyps, and asthma were significantly associated with postoperative recurrence, while Rosati D et al. [27] pointed out that the long-term postoperative recurrence of CRSwNP was closely correlated with high-level eosinophil infiltration and high interleukin (IL)-5 expression.

Multivariate analysis confirmed that the Davos score of nasal polyps, postoperative infection, ECP/MPO, IgE, and CCL4 were prominent risk factors for the postoperative recurrence of CRSwNP. In a prospective study by Brescia G et al. [28], it was also noted that eosinophilic CRSwNP was independently associated with postoperative recurrence in CRSwNP patients. Meanwhile, considering the influences of IgE and CCL4 on the potential pathological process of CRSwNP, we hypothesize that these two factors may, to some extent, mediate pre-existing and postoperative infections in CRSwNP patients. Further in-depth exploration and verification through relevant research in the future are thus warranted. Finally, a nomogram was developed based on these variables to predict the risk of postoperative recurrence. Clinically, for CRSwNP patients with a high Davos score of nasal polyps, presence of postoperative infection, and high levels of ECP/MPO, IgE, and CCL4, the adjustment of treatment strategies or the enhancement of targeted preventive care for postoperative infection should be considered to further reduce the postoperative relapse risk of CRSwNP patients.

This study has several limitations that warrant attention in future research. First, the duration of postoperative infections was not quantified, which limits our understanding of its precise relationship with CRSwNP recurrence. A more detailed analysis of infection duration would help clarify this link. Second, while ECP/MPO has been suggested as a potential nasal secretion indicator for CRS endotype diagnosis, further investigation into pre- and post-surgical levels of ECP/MPO in CRSwNP patients could help elucidate its clinical advantages and potential applications. Third, the time interval between surgery and relapse was not incorporated into our analysis, but this data would provide additional insights into the timing of postoperative recurrence. Finally, research into the molecular mechanisms linking IgE and CCL4 to pre- and postoperative infections in CRSwNP patients is needed to clarify their role in the recurrence process.

In summary, ECP/MPO, IgE, and CCL4 appear to play a significant role in mediating the postoperative recurrence mechanism in CRSwNP patients. When used in combination, these three biomarkers demonstrate strong diagnostic performance in predicting postoperative relapse. Additionally, they are identified as key risk factors for postoperative recurrence, alongside the Davos score of nasal polyps and postoperative infection. Our study offers valuable insights and reliable evidence for predicting the postoperative relapse of CRSwNP in patients and presents a quantitative tool for predicting the risk of postoperative recurrence in such patients.

Disclosure of conflict of interest

None.

Address correspondence to: Wenshuai Chang, Department of Otolaryngology, Air Force Hospital of The Central Theater Command of PLA, Datong 037006, Shanxi, China. Tel: +86-0352-5385260; E-mail: 13133325033@163.com

References

[1] Ma L, Shi J, Wang K, Sun Y and Xu R. Clinical characteristics of patients with CRSwNP with intensely high eosinophil level. Laryngoscope Investig Otolaryngol 2022; 7: 316-324.

[2] Shen Y, Ke X, Hong S and Yang Y. Adverse events for biologics in patients with CRSwNP: a meta-analysis. Clin Transl Allergy 2022; 12: e12169.

[3] Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, Toppila-Salmi S, Bernal-Sprekelsen M, Mullol J, Alobid I, Terezinha Anselmo-Lima W, Bachert C, Baroody F, von Buchwald C, Cervin A, Cohen N, Constantinidis J, De Gabory L, Desrosiers M, Diamant Z, Douglas RG, Gevaert PH, Hafner A, Harvey RJ, Joos GF, Kalogjera L, Knill A, Kocks JH, Landis BN, Limpens J, Lebeer S, Lourenco O, Meco C, Matricardi PM, O'Mahony L, Philpott CM, Ryan D, Schlosser R, Senior B, Smith TL, Teeling T, Tomazic PV, Wang DY, Wang D, Zhang L, Agius AM, Ahlstrom-Emanuelsson C, Alabri R, Albu S, Alhabash S, Aleksic A, Aloulah M, Al-Qudah M, Alsaleh S, Baban MA, Baudoin T, Balvers T, Battaglia P, Bedoya JD, Beule A, Bofares KM, Braverman I, Brozek-Madry E, Richard B, Callejas C, Carrie S, Caulley L, Chussi D, de Corso E, Coste A, El Hadi U, Elfarouk A, Eloy PH, Farrokhi S, Felisati G, Ferrari MD, Fishchuk R, Grayson W, Goncalves PM, Grdinic B, Grgic V, Hamizan AW, Heinichen JV, Husain S, Ping TI, Ivaska J, Jakimovska F, Jovancevic L, Kakande E, Kamel R, Karpischenko S, Kariyawasam HH, Kawauchi H, Kjeldsen A, Klimek L, Krzeski A, Kopacheva Barsova G, Kim SW, Lal D, Letort JJ, Lopatin A, Mahdjoubi A, Mesbahi A, Netkovski J, Nyenbue Tshipukane D, Obando-Valverde A, Okano M, Onerci M, Ong YK, Orlandi R, Otori N, Ouennoughy K, Ozkan M, Peric A, Plzak J, Prokopakis E, Prepageran N, Psaltis A, Pugin B, Raftopulos M, Rombaux P, Riechelmann H, Sahtout S, Sarafoleanu CC, Searyoh K, Rhee CS, Shi J, Shkoukani M, Shukuryan AK, Sicak M, Smyth D, Sindvongs K, Soklic Kosak T, Stjarne P, Sutikno B, Steinsvag S, Tantilipikorn P, Thanaviratananich S, Tran T, Urbancic J, Valiulius A, Vasquez de Aparicio C, Vicheva D, Virkkula PM, Vicente G, Voegels R, Wagenmann MM, Wardani RS, Welge-Lussen A, Witterick I, Wright E, Zabolotniy D, Zsolt B and Zwetsloot CP. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology 2020; 58 Suppl S29: 1-464.

[4] Bhattacharyya N, Villeneuve S, Joish VN, Amand C, Mannent L, Amin N, Rowe P, Maroni J, Eckert L, Yang T and Khan A. Cost burden and resource utilization in patients with chronic rhinosinusitis and nasal polyps. Laryngoscope 2019; 129: 1969-1975.

[5] Stevens WW, Schleimer RP and Kern RC. Chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract 2016; 4: 565-572.

[6] Bandi S, Stephen E, Bansal K and Mahdavinia M. Understanding the CRSwNP patient as whole. Am J Rhinol Allergy 2023; 37: 140-146.

[7] Sanchez-Collado I, Mora T, Munoz-Cano R, Ribo P, Mullol J and Valero A. Prevalence of chronic rhinosinusitis with nasal polyps in catalonia (spain): a retrospective, large-scale population-based study. Rhinology 2022; 60: 384-396.

[8] Veloso-Teles R and Cerejeira R. Endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps: clinical outcome and predictive factors of recurrence. Am J Rhinol Allergy 2017; 31: 56-62.

[9] Munthe-Kaas MC, Gerritsen J, Carlsen KH, Undlien D, Egeland T, Skinningsrud B, Torres T and Carlsen KL. Eosinophil cationic protein (ECP) polymorphisms and association with asthma, s-ECP levels and related phenotypes. Allergy 2007; 62: 429-436.

[10] Bystrom J, Patel SY, Amin K and Bishop-Bailey D. Dissecting the role of eosinophil cationic protein in upper airway disease. Curr Opin Allergy Clin Immunol 2012; 12: 18-23.

[11] Aratani Y. Myeloperoxidase: its role for host defense, inflammation, and neutrophil function. Arch Biochem Biophys 2018; 640: 47-52.

[12] Jin J, Guo B, Zhang W, Chen JJ, Deng YQ, Xiang R, Tan L, Qin DX, Zheng L, Chen Z, Tao ZZ and Xu Y. Diagnostic value of myeloperoxidase and eosinophil cationic protein in nasal secretions for endotypes of chronic rhinosinusitis. Eur Arch Otorhinolaryngol 2023; 280: 3707-3720.

[13] Bachert C, Gevaert P, Holtappels G, Johansson SG and van Cauwenberge P. Total and specific IgE in nasal polyps is related to local eosinophilic inflammation. J Allergy Clin Immunol 2001; 107: 607-614.

[14] Perrin-Cocon L, Agaugue S, Diaz O, Vanbervliet B, Dollet S, Guironnet-Paquet A, Andre P and Lotteau V. Th1 disabled function in response to TLR4 stimulation of monocyte-derived DC from patients chronically-infected by hepatitis C virus. PLoS One 2008; 3: e2260.

[15] Chu HH, Kobayashi Y, Bui DV, Yun Y, Nguyen LM, Mitani A, Suzuki K, Asako M, Kanda A and Iwai H. CCL4 regulates eosinophil activation in eosinophilic airway inflammation. Int J Mol Sci 2022; 23: 16149.

[16] Bhattacharyya N and Lee LN. Evaluating the diagnosis of chronic rhinosinusitis based on clinical guidelines and endoscopy. Otolaryngol Head Neck Surg 2010; 143: 147-151.

[17] Gevaert P, De Craemer J, Bachert C, Blauwblomme M, Chaker A, Cingi C, Hellings PW, Hopkins C, Hox V, Fokkens WJ, Klimek L, Lund V, Mosges R, Mullol J, Pfaar O, Scadding G, Tomazic PV, Van Zele T, Vlaminck S, Wagenmann M, Toppila-Salmi S and Alobid I. European academy of allergy and clinical immunology position paper on endoscopic scoring of nasal polyposis. Allergy 2023; 78: 912-922.

[18] Asghari M, Izadpanahi S and Esfahani MH. Comparison of blood and tissue eosinophil count and blood IgE in patients with chronic

sinusitis and nasal polyps. J Immunol Res 2021; 2021: 6680676.
[19] Wang LF, Lee CH, Chien CY, Chen JY, Chiang FY and Tai CF. Serum 25-hydroxyvitamin D levels are lower in chronic rhinosinusitis with nasal polyposis and are correlated with disease severity in Taiwanese patients. Am J Rhinol Allergy 2013; 27: e162-165.
[20] Van Zele T, Holtappels G, Gevaert P and Bachert C. Differences in initial immunoprofiles between recurrent and nonrecurrent chronic rhinosinusitis with nasal polyps. Am J Rhinol Allergy 2014; 28: 192-198.
[21] Zheng M, Wang M, Li Y, Wang XD and Zhang L. Expression of immunological and inflammatory biomarkers in chronic rhinosinusitis with nasal polyps and its predictive value for recurrence. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2019; 54: 174-180.
[22] Grgic MV, Cupic H, Kalogjera L and Baudoin T. Surgical treatment for nasal polyposis: predictors of outcome. Eur Arch Otorhinolaryngol 2015; 272: 3735-3743.
[23] Krzeski A, Galewicz A, Chmielewski R and Kisiel M. Influence of cigarette smoking on endoscopic sinus surgery long-term outcomes. Rhinology 2011; 49: 577-582.
[24] Matsuwaki Y, Ookushi T, Asaka D, Mori E, Nakajima T, Yoshida T, Kojima J, Chiba S, Ootori N and Moriyama H. Chronic rhinosinusitis: risk factors for the recurrence of chronic rhinosinusitis based on 5-year follow-up after endoscopic sinus surgery. Int Arch Allergy Immunol 2008; 146 Suppl 1: 77-81.
[25] Vlaminck S, Acke F, Prokopakis E, Speleman K, Kawauchi H, van Cutsem JC, Hellings PW, Jorissen M, Seys S, Bachert C, Zele TV, Lambrecht BN and Gevaert P. Surgery in nasal polyp patients: outcome after a minimum observation of 10 years. Am J Rhinol Allergy 2021; 35: 449-457.
[26] Fageeh YA, Basurrah MA, Hakami KT, Almalki ZA, Alnemari FS and Altalhi WA. Risk factors for recurrence of chronic rhinosinusitis with nasal polyps after endoscopic sinus surgery: a retrospective study. Saudi Med J 2023; 44: 1254-1259.
[27] Rosati D, Rosato C, Pagliuca G, Cerbelli B, Della Rocca C, Di Cristofano C, Martellucci S and Gallo A. Predictive markers of long-term recurrence in chronic rhinosinusitis with nasal polyps. Am J Otolaryngol 2020; 41: 102286.
[28] Brescia G, Marioni G, Franchella S, Ramacciotti G, Giacomelli L, Marino F and Martini A. A prospective investigation of predictive parameters for post-surgical recurrences in sinonasal polyposis. Eur Arch Otorhinolaryngol 2016; 273: 655-660.