Turkish Archives of Otorhinolaryngology

Original Investigation

Turk Arch Otorhinolaryngol
DOI: 10.4274/tao.2026.2025-10-11

Role of Nasal Nitric Oxide in the Diagnosis of Epithelial Remodeling Types of Nasal Polyps

Xu Liang, Hongyang Zhang, Peng Jin, Li Zhao, Xiaoxue Zi, Kena Yu, Li Shi

The Second Qilu Hospital of Shandong University, Department of Otorhinolaryngology, Head and Neck Surgery, Shandong, China

Abstract

Objective: The aim of this study is to investigate the clinical application value of exhaled nasal nitric oxide (nNO) in the pathological diagnosis and classification of epithelial remodeling in nasal polyps (NP).

Methods: The differences between the nNO levels in patients with NP exhibiting different types of epithelial remodeling and the correlations between nNO and clinical data were retrospectively analyzed. The diagnostic value of nNO in NP was evaluated using receiver operating characteristic curves.

Results: The levels of nNO in the control group were found to be significantly higher than those in the epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia groups (p=0.001, p=0.001, p=0.02). Furthermore, the levels were found to be significantly higher in the squamous metaplasia group than those in the epithelial hyperplasia and goblet cell hyperplasia groups (p=0.025, p=0.018). The percentage and count of eosinophils in peripheral blood in the goblet cell hyperplasia group were significantly higher than in the control group (p=0.001). nNO levels were negatively correlated with the ethmoid-to-maxillary computed tomography score ratio (E/M ratio) and Lund-Mackay score (L-M score) in the epithelial hyperplasia group and the goblet cell hyperplasia group (r=-0.518, p<0.05; r=-0.640, p<0.01; r=-0.421, p<0.01; r=-0.599, p<0.001, respectively). Similarly, a negative correlation was identified between nNO levels and the L-M score in the squamous metaplasia group (r=-0.612, p<0.01). nNO levels exhibited moderate diagnostic value in differentiating non-chronic sinusitis patients from epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia [area under the curve (AUC) =0.898, p<0.001; AUC=0.882, p<0.001; AUC=0.720, p=0.025, respectively].

Conclusion: nNO has been shown to have significant clinical value in the preliminary pathological diagnosis and prediction of NP lesions with nasal epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia.

Keywords: Nasal polyps, sinusitis, nitric oxide, cell differentiation, metaplasia, goblet cells, receiver operating characteristic curve

ORCID IDs of the authors:
X.L. 0000-0001-6297-962X
H.Z. 0000-0003-4136-8090
P.J. 0000-0002-5696-2095
L.Z. 0000-0003-1777-0493
X.Z. 0000-0002-2752-1442
K.Y. 0000-0003-1638-7468
L.S. 0000-0002-4162-7876

Cite this article as: *Liang X, Zhang H, Jin P, Zhao L, Zi X, Yu K, et al. Role of nasal nitric oxide in the diagnosis of epithelial remodeling types of nasal polyps. Turk Arch Otorhinolaryngol. [Epub Ahead of Print]*

Corresponding Author:
Li Shi, Prof.;
shili126@sina.com

Received Date: 24.10.2025
Accepted Date: 06.01.2026
Epub: 15.04.2026

Introduction

Chronic sinusitis (CRS) is a common chronic inflammatory disease of the nasal cavity and paranasal sinuses, caused by the interaction of multiple factors, including environmental and host-related factors (1). Nasal polyps (NP) are a type of CRS characterized by inflammation and benign hyperplasia of the mucosa of the nasal cavity and nasal sinuses (2). The respiratory mucosa of the nasal cavity and sinuses is covered by pseudostratified ciliated columnar epithelium, while the anterior nasal cavity is covered by squamous epithelium (3). The airway epithelial barrier, composed of a mucous layer overlying the ciliated epithelium, is important in heating and humidifying the air and maintaining the host's innate immune defense (3). The epithelial tissue in type 2 immune-mediated inflammatory states has been found to exhibit barrier dysfunction, characterized by decreased epithelial cell diversity due to abnormal differentiation of basal cells (4). Therefore, environmental and intrinsic signals enable epithelial basal progenitor cells to proliferate and differentiate into ciliated and goblet cells or undergo squamous metaplasia, thereby rapidly changing the composition and function of the epithelium, which may play an important role in the pathogenesis of CRS (5).

Nitric oxide (NO) is a colorless, odorless gas found in the human body in a variety of cells, including epithelial cells, nerve cells, endothelial cells, and inflammatory cells. Inducible NO synthase (iNOS) produces NO from L-arginine and is mainly expressed in respiratory epithelial cells and immune cells involved in respiratory inflammation. Proinflammatory factors can induce NO production by iNOS. Therefore, NO is an important marker of respiratory inflammation (6). In the upper respiratory tract, nasal NO (nNO) is produced mainly by the mucous membranes of the nasal passages and the sinuses (7). Our team's previous study found that epithelial remodeling in NP predominantly presents as three types: epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia (6). Therefore, exploring the differences in nNO levels among different types of epithelial tissue remodeling has important clinical value for predicting epithelial remodeling types and improving the accuracy of CRS diagnosis.

Methods

Patients

CRS patients with NP (CRSwNP) (n=85) who underwent endoscopic nasal surgery were identified in the The Second Qilu Hospital of Shandong University from January 2024 to March 2025. Subjects (n=28) with symptomatic nasal septal deviation requiring septoplasty surgery served as controls. None of the controls had chronic rhinosinusitis with or without NP at computed tomography (CT) examination. CRSwNP diagnosis was made based on history taking, physical examination, nasal endoscopic examination, and CT findings of the sinuses according to the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (1). The inclusion criteria of the control group were no smoking history, no history of CRS, allergic rhinitis (AR), or asthma; no abnormal nasal secretions, polyps, or other masses, normal blood routine, normal serum immunoglobulin E (IgE) level, and normal lung function. Exclusion criteria: under 18 years of age, presence of cystic fibrosis, ciliary immobility syndrome, aspirin intolerance triad, immunodeficiency disease, severe systemic disease, respiratory infection in the last month, menstruation, or pregnancy. Ethical approval was obtained from the Ethics Committee of the Second Hospital of Shandong University (approval number: KYLL-2018(KJ)P-0025, date: 26.02.2018). The written consent from all subjects was obtained.

Clinical Data

The diagnosis of AR is determined by the Allergic Rhinitis and Its Impact on Asthma and European Academy of Allergy and Clinical Immunology guidelines (clinical symptoms, such as nasal obstruction, rhinorrhea, sneezing, and nasal itching; and objective evidence of allergic sensitization, including serum allergen-specific IgE) (8). The diagnosis of asthma is made according to the results of the pulmonary function relaxation test or by a respiratory doctor. The percentage of eosinophils in peripheral blood and the count of eosinophils were detected using the XN9000 RapidBio blood analyzer. The CT scans were scored according to the Lund-Mackay score system, and the ratio of the total score of both ethmoid sinuses to the total score of the maxillary sinuses (E/M ratio) was calculated (9,10).

The nNO Test

The nNO test was sampled, analyzed, and automatically generated using the breath analyzer Sunvou-CA2122 (Sunvou Medical Electronics, Wuxi, China). After 30 minutes of rest, the patient was placed in a seated position, and the relatively unobstructed nostril was closed with a nasal plug, while the other nostril was kept unobstructed. Then a whistle was placed in the patient's mouth, and the patient was asked to continuously blow after a deep inhalation without breath-holding. The air pump of the instrument was used to aspirate air from the nostril at a constant flow rate of 10 mL/s. The NO gas produced in the nasal cavity and sinuses was collected from the nasal cavity by this airflow. Whistling was used to ensure velum closure and prevent contamination from the lower respiratory tract during nasal sampling. After sampling was completed, the instrument analyzed the sample and automatically generated the results.

Tissue Samples

NP tissue samples were fixed in 10% formalin, embedded in paraffin, and stained with hematoxylin and eosin for histological analysis. The epithelial cell hyperplasia, goblet cell hyperplasia and squamous metaplasia of NP tissue were evaluated under optical microscope according to the results of hematoxylin and eosin staining. It was defined as normal epithelium or no epithelial hyperplasia when the epithelial surface of NP tissue had no obvious hyperplasia, or the number of epithelial layers was ≤4 (Figure 1). It was defined as epithelial hyperplasia when the epithelial surface of NP tissue was ≥4 (Figure 2). Goblet cell hyperplasia was defined when the number of goblet cell layers on the epithelial surface was ≥2 (Figure 3). Squamous metaplasia was defined when the normal pseudostratified ciliated columnar epithelium disappeared and the ciliated cells and goblet cells on the epithelial surface were completely replaced by squamous cells (Figure 4) (11).

Statistical Analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Mean ± standard deviation was used for the descriptive statistics of continuous variables. The independent samples t-test and χ^2 test were used to evaluate differences between groups for variables conforming to a normal distribution, and the Mann-Whitney U test was used for variables not conforming to a normal distribution. Spearman's correlation coefficient was used to analyze the correlation between nNO and clinical data. The predictive value of nNO for CRS was analyzed using the receiver

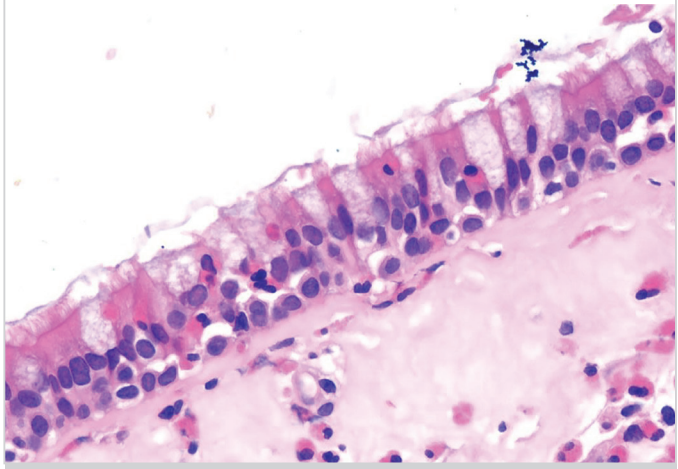

Figure 1. Type of epithelium: normal epithelium (H&E staining ×400)
H&E: Hematoxylin and eosin

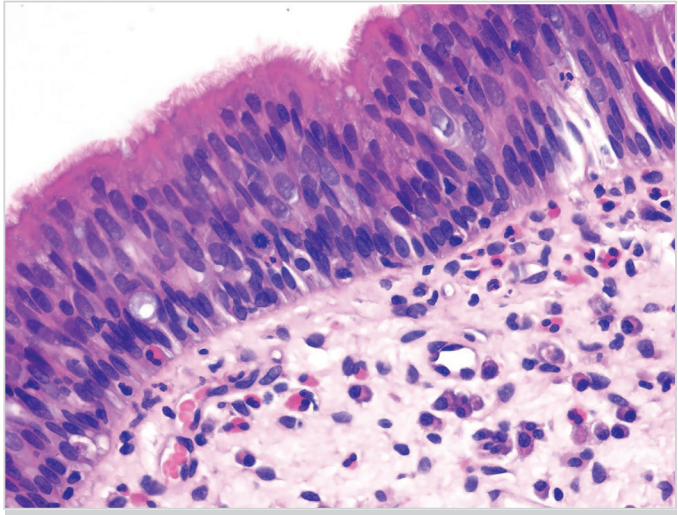

Figure 2. Type of epithelium: epithelial hyperplasia (H&E staining x400)
H&E: Hematoxylin and eosin

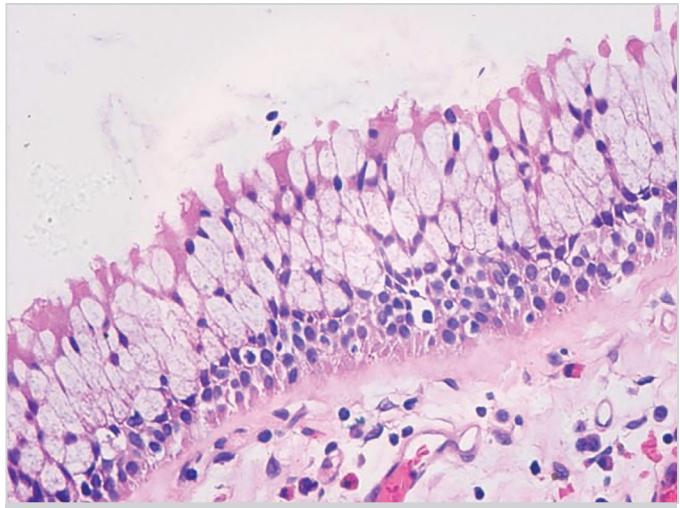

Figure 3. Type of epithelium: goblet cell hyperplasia (H&E staining ×400)
H&E: Hematoxylin and eosin

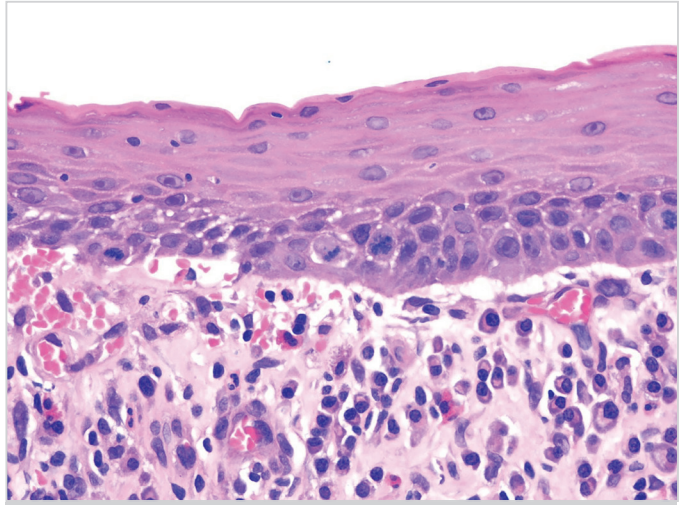

Figure 4. Type of epithelium: squamous metaplasia (H&E staining ×400)
H&E: Hematoxylin and eosin

operating characteristic (ROC) curve. A p-value of <0.05 was considered to indicate statistical significance.

Results

Comparison of Clinical Data

Of the 85 CRSwNP patients, 25 had epithelial hyperplasia, 47 had goblet cell hyperplasia, and 13 had squamous metaplasia based on histological analysis. There was no significant difference in gender among the various groups of patients. The mean age of the epithelial hyperplasia group was significantly higher than that of the control group (p=0.01). The percentage and absolute count of peripheral blood eosinophils in the goblet cell hyperplasia group were significantly higher than those of the control group (p=0.01). In contrast, the nNO level was significantly higher in the control group compared to the epithelial cell hyperplasia, goblet cell hyperplasia, and squamous metaplasia groups (p=0.001, p=0.001, p=0.02). There were no significant differences in terms of gender, smoking history, or body mass index (p>0.05) (Table 1).

nNO Levels in the Group of Epithelial Remodeling Types

The mean nNO levels in the squamous metaplasia group were significantly higher than those in both the epithelial hyperplasia and goblet cell hyperplasia groups (p=0.025, p=0.018). However, there were no significant differences in nNO levels between the epithelial hyperplasia and goblet cell hyperplasia groups (p=0.78) (Figure 5).

Correlations Between nNO Levels and Clinical Data

In the epithelial hyperplasia and goblet cell hyperplasia groups, nNO levels were negatively correlated with both the E/M ratio and the Lund-Mackay score (epithelial hyperplasia: r=-0.518, p<0.05; r=-0.640, p<0.01; goblet cell hyperplasia: r=-0.421, p<0.01; r=-0.599, p<0.001, respectively). In the squamous metaplasia group, nNO levels were negatively correlated with the Lund-Mackay score (r=-0.612, p<0.01), but showed no significant correlation with the E/M ratio (p>0.05). No significant correlations were found between nNO levels and age, body mass index, peripheral blood eosinophil percentage, or eosinophil count in any of the groups (control, epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia) (p>0.05) (Table 2).

ROC Curve Analysis

ROC curve analysis demonstrated that nNO had moderate diagnostic performance in distinguishing non-CRS subjects from those with epithelial hyperplasia, goblet cell hyperplasia, or squamous metaplasia [area under the curve (AUC) =0.898, p<0.001; AUC=0.882, p<0.001; and AUC=0.720, p=0.025, respectively] (Figure 6).

Discussion

With the lucubration of the research on the pathogenesis of CRS, more and more attention has been paid to the role of epithelial barrier damage and epithelial tissue remodeling in the pathogenesis of CRS. Tissue remodeling is an abnormal manifestation of tissue injury and has been extensively

Table 1. Comparison of clinical characteristics among the study groups

	Control	Epithelial hyperplasia	Goblet cell hyperplasia	Squamous metaplasia	p-value	p-value	p-value
	(n=28); 1	(n=25); 2	(n=47); 3	(n=13); 4	(1 vs. 2)	(1 vs. 3)	(1 vs. 4)
Male/female	20/8	18/7	34/13	7/6	0.96	0.93	0.27
Smoking, n (%)	7 (25)	9 (36)	14 (29.8)	5 (38.5)	0.38	0.66	0.38
Allergic, n (%)	—	4 (16)	13 (27.7)	5 (38.5)	—	—	—
Asthma, n (%)	—	3 (12)	10 (21.3)	1 (7.7)	—	—	—
Recurrence, n (%)	—	5 (20)	8 (17.0)	1 (7.7)	—	—	—
eCRSwNP, n (%)	—	12 (48)	37 (78.7)	9 (69.2)	—	—	—
Age, years	41.39±13.85	51.48±11.53	46.91±11.02	42.38±13.41	0.01	0.08	0.88
BMI (kg/m^2)	25.08±4.12	25.62±4.00	26.35±2.85	25.22±3.64	0.54	0.23	0.95
EOS percentage, %	2.86±2.84	4.00±3.34	5.10±3.59	4.33±3.99	0.14	0.01	0.60
EOS count (x10^{-9}•L^{-1})	0.17±0.14	0.24±0.19	0.33±0.22	0.28±0.26	0.15	0.00	0.52
E/M ratio	—	1.52±0.92	2.33±1.08	1.42±1.24	—	—	—
Lund-Mackay score	—	13.78±8.12	15.89±5.64	13.23±6.80	—	—	—
nNO (ppb)	428.7±121.2	214.5±114.1	222.0±127.9	331.4±151.8	0.00	0.00	0.02

eCRSwNP: Eosinophilic chronic rhinosinusitis with nasal polyps, BMI: Body mass index, EOS: Blood eosinophil, E/M ratio: Ratio of the computed tomography scores for the ethmoid sinus and maxillary sinus, nNO: Nasal nitric oxide, ppb: Part per billion

studied in lower respiratory diseases, as well as in CRS. Tissue eosinophilia and eosinophilia activation were found to be significantly correlated with CRS remodeling features, associated mucosal injury, and clinical symptoms (12).

In recent years, people have come to realize that NO is not only an environmental pollutant but also a biological medium, playing a significant role in regulating physiological processes such as vascular dilation and cardiovascular systems in both animals and humans (13). As a pro-inflammatory medium NO increases susceptibility to airway hyperreactivity in humans and plays a very complex role in the pathophysiology of airway response (14). At present, FeNO has been widely used in clinical diagnosis and efficacy evaluation, and monitoring of asthma (15). nNO is produced mainly by the mucous membranes of the nasal cavity and the nasal sinuses but the relationship between its level and the mucosal epithelial status of the nasal cavity and nasal sinuses is not clear.

When we grouped the types of polyp epithelial remodeling in CRSwNP patients, we found that nNO levels in the squamous metaplasia group were significantly higher than those in the epithelial hyperplasia and goblet cell hyperplasia groups. Pasto et al. (16) found that NO played a significant role in stimulating ciliary movement in the respiratory tract, and the increase of nNO level in squamous CRSwNP patients could be related to the increased feedback of NO production due to the loss of ciliary structure. Cilia are hair-like organelles composed of microtubules. The nose and sinuses use the connecting complex between the mucociliary clearance system and the epithelial cells as their first line of defense against the environment (17). Li et al. (18) found that cilia structure and function were abnormal in patients with CRSwNP. The injury of motor cilia was accompanied by epithelial hyperplasia and other epithelial cell changes, which may be the cause of chronic mucosal inflammation or infection in patients with CRS (18). Ma et al. (19) reported that compared with the control group, the expression of ciliogenic protein in the sinus epithelium of CRS patients with ciliated deletion was significantly reduced. Overall, epithelial barrier remodeling caused by ciliary dysfunction in CRSwNP patients can cause changes in nNO levels. We can preliminarily determine the remodeling type of epithelial tissue and ciliary changes of CRSwNP by nNO.

ROC curve analysis showed that nNO had moderate predictive value in differentiating non-CRS from epithelial

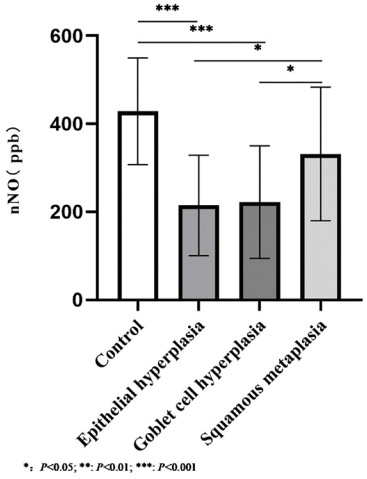

Figure 5. Comparison of nNO among epithelial remodeling groups
nNO: Nasal nitric oxide, ppb: Part per billion

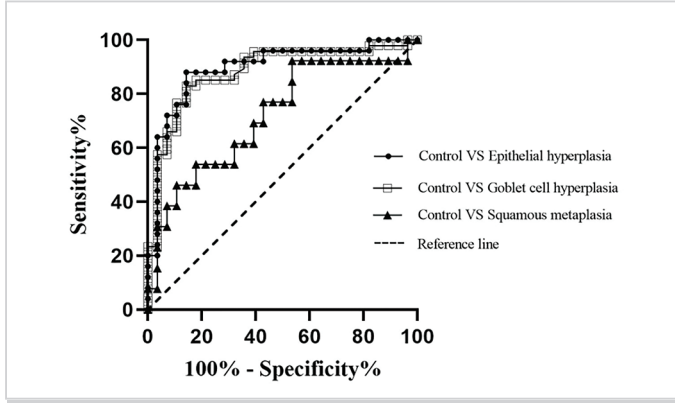

Figure 6. ROC curve of nNO for the diagnosis of epithelial hyperplasia, goblet cell hyperplasia, and squamous metaplasia
ROC: Receiver operating characteristic, nNO: Nasal nitric oxide

Table 2. Correlation of nNO with clinical data in epithelial type group

	Control	Epithelial hyperplasia	Goblet cell hyperplasia	Squamous metaplasia
	r	r	r	r
Age	0.304	-0.127	-0.171	-0.0469
BMI (kg/m^2)	0.170	0.171	-0.177	-0.555
EOS percentage, %	-0.136	0.278	-0.185	0.277
EOS count (x10-9•L-1)	-0.157	0.296	-0.161	0.197
E/M ratio	—	-0.518*	-0.421**	-0.344
Lund-Mackay score	—	-0.640**	-0.599***	-0.612*

*: p<0.05, **: p<0.01, ***: p<0.001, BMI: Body mass index, EOS percentage: Blood eosinophil percentage, EOS count: Blood eosinophil count, E/M ratio: Ratio of the computed tomography scores for the ethmoid sinus and maxillary sinus

hyperplasia, goblet cell hyperplasia, and squamous cell metaplasia. Therefore, nNO has certain clinical application value in predicting the epithelial remodeling type of NP. CRS is a heterogeneous disease with multiple inflammatory mechanisms involved and inflammatory progression. The specific histopathological differentiation between CRSwNP and CRSsNP patients is still difficult to clearly identify (20). The histopathological features of CRSwNP are related to the severity of the prognosis, and we need to further explore the relationship between histopathological features of CRSwNP and disease progression.

In recent years, the remodeling of the epithelial barrier has aroused great interest among researchers. The occurrence of tissue remodeling is caused by the joint action of inflammation and related cytokines, regulatory factors, enzymes and other factors, which in turn determine the type of tissue remodeling (21). Studies have attempted to correlate cytokines and other tissue markers with tissue remodeling changes, such as periosteal protein, transforming growth factor-β, and interleukin-13, with basement membrane thickening and fibrosis (22). We can preliminarily predict the type of epithelial tissue remodeling of CRSwNP through the study of nNO, which is of great value for the clinical diagnosis and treatment of CRSwNP. We found that epithelial changes play an increasingly crucial role in the pathogenesis of CRSwNP with the in-depth study of the mechanisms related to epithelial tissue remodeling. However, the related mechanism remains to be further studied.

Study Limitations

Due to the relatively small sample size, the exact reference value of nNO for the accurate diagnosis of CRSwNP needs to be further studied, and our conclusion also needs to be expanded for further verification and in-depth study. It will be necessary in the future to further increase the sample size to eliminate the influence of factors such as age. We did not conduct the nasal patency test, which might have affected the relevant results.

Conclusion

In conclusion, the nNO test has become simple and can be used as a biological marker in the evaluation of nasal inflammatory diseases with the advancement of technology and the implementation of standardization work. As a quantitative, non-invasive, convenient and safe tool, the nNO test has certain clinical application value in predicting the type of epithelial remodeling of NP.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of the Second Hospital of Shandong University (approval number: KYLL-2018(KJ) P-0025, date: 26.02.2018).

Informed Consent: The written consent from all subjects was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: P.J., L.Z., X.Z., K.Y., L.S., Concept: L.S., Design: X.L., L.S., Data Collection and/or Processing: X.L., H.Z., Analysis or Interpretation: X.L., H.Z., Literature Search: X.L., H.Z., L.S., Writing: X.L., L.S.

Conflict of Interest: The authors declare that they have no conflict of interest.

Financial Disclosure: This research was supported by National Natural Science Foundation of China (82371117) and National Natural Science Foundation of China (82101195).

Main Points

- The nasal nitric oxide (nNO) levels in control group was significantly higher than that of epithelial hyperplasia, goblet cell hyperplasia and squamous metaplasia groups ($p<0.05$), and squamous metaplasia group was significantly higher than that in epithelial hyperplasia group and goblet cell hyperplasia group ($p<0.05$).
- The percentage and count of eosinophilia in peripheral blood of goblet cell hyperplasia group was significantly higher than that of control group ($p<0.05$).
- The nNO levels was negatively correlated with E/M ratio and Lund-Mackay score in epithelial hyperplasia group and goblet cell hyperplasia group ($r=-0.518$, $p<0.05$; $r=-0.640$, $p<0.01$; $r=-0.421$, $p<0.01$; $r=-0.599$, $p<0.001$), and nNO levels in squamous cell metaplasia group was negatively correlated with Lund-Mackay score ($r=-0.612$, $p<0.01$).
- The nNO levels was moderately valuable in differentiating non-chronic sinusitis from epithelial hyperplasia, goblet cell hyperplasia, and squamous cell metaplasia [area under the curve (AUC) =0.898, $p<0.001$; AUC=0.882, $p<0.001$; AUC=0.720, $p=0.025$].

References

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology. 2020; 58: 1-464. [Crossref]
2. Kwah JH, Peters AT. Nasal polyps and rhinosinusitis. Allergy Asthma Proc. 2019; 40: 380-4. [Crossref]
3. Rayamajhi D, Ege M, Ukhanov K, Ringers C, Zhang Y, Jung I, et al. The forkhead transcription factor Foxj1 controls vertebrate olfactory cilia biogenesis and sensory neuron differentiation. PLoS Biology. 2024; 22: e3002468. Erratum in: PLoS Biol. 2025; 23: e3003229. [Crossref]
4. Ordovas-Montanes J, Dwyer DF, Nyquist SK, Buchheit KM, Vukovic M, Deb C, et al. Allergic inflammatory memory in human respiratory epithelial progenitor cells. Nature. 2018; 560: 649-54. [Crossref]

5. Yan B, Lan F, Li J, Wang C, Zhang L. The mucosal concept in chronic rhinosinusitis: focus on the epithelial barrier. J Allergy Clin Immunol. 2024; 153: 1206-14. [Crossref]
6. Kawasumi T, Takeno S, Ishikawa C, Takahara D, Taruya T, Takemoto K, et al. The functional diversity of nitric oxide synthase isoforms in human nose and paranasal sinuses: contrasting pathophysiological aspects in nasal allergy and chronic rhinosinusitis. Int J Mol Sci. 2021; 22: 7561. [Crossref]
7. Spector BM, Shusterman DJ, Zhao K. Nasal nitric oxide flux from the paranasal sinuses. Curr Opin Allergy Clin Immunol. 2023; 23: 22-8. [Crossref]
8. Bousquet J, Schünemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation allergic rhinitis and its impact on asthma (ARIA) guidelines for allergic rhinitis based on grading of recommendations assessment, development and evaluation (GRADE) and real-world evidence. J Allergy Clin Immunol. 2020; 145: 70-80. Erratum in: J Allergy Clin Immunol. 2022; 149: 2180. [Crossref]
9. Lund VJ, Mackay IS. Staging in rhinosinusitus. Rhinology. 1993; 31: 183-4. [Crossref]
10. Wu PW, Wei ZH, Huang CC, Chang PH, Lee TJ, Huang CC. Predictive value of computed tomographic ethmoid-to-maxillary ratio in patients with chronic rhinosinusitis and nasal polyp. J Asthma Allergy. 2025; 18: 1167-77. [Crossref]
11. Chen Z, Peng Y, Ng CL, Jin P, Liu J, Li YY, et al. The clinical characteristics and histopathological features of chronic rhinosinusitis with unilateral nasal polyps in 136 patients in Southern China. Clin Otolaryngol. 2018; 43: 1345-9. [Crossref]
12. Siddiqui S, Bachert C, Bjermer L, Buchheit KM, Castro M, Qin Y, et al. Eosinophils and tissue remodeling: relevance to airway disease. J Allergy Clin Immunol. 2023;152: 841-57. [Crossref]
13. Palmer RM, Ashton DS, Moncada S. Vascular endothelial cells synthesize nitric oxide from L-arginine. Nature. 1988; 333: 664-6. [Crossref]
14. Wang F, Liu Z, Li WX, Wang XM, Yang J, Zhao ZH, et al. Nitric oxide synthase inhibitors reduce the formation of neutrophil extracellular traps and alleviate airway inflammation in the mice model of asthma. Naunyn Schmiedebergs Arch Pharmacol. 2025; 398: 8963-73. [Crossref]
15. Task Force for Pulmonary Function of Chinese Thoracic Society. Chinese expert consensus on the testing process and clinical application of fractional exhaled nitric oxide detector (2025). International Journal of Respiration. 2025; 45: 369-81. [Crossref]
16. Pasto M, Serrano E, Urocoste E, Barbacanne MA, Guissani A, Didier A, et al. Nasal polyp-derived superoxide anion: dose-dependent inhibition by nitric oxide and pathophysiological implications. Am J Respir Crit Care Med. 2001; 163:145-51. [Crossref]
17. Toppila-Salmi S, van Drunen CM, Fokkens WJ, Golebski K, Mattila P, Joenvaara S, et al. Molecular mechanisms of nasal epithelium in rhinitis and rhinosinusitis. Curr Allergy Asthma Rep. 2015; 15: 495. [Crossref]
18. Li YY, Li CW, Chao SS, Yu FG, Yu XM, Liu J, et al. Impairment of cilia architecture and ciliogenesis in hyperplastic nasal epithelium from nasal polyps. J Allergy Clin Immunol. 2014; 134: 1282-92. [Crossref]
19. Ma Y, Sun Y, Jiang L, Zuo K, Chen H, Guo J, et al. WDPCP regulates the ciliogenesis of human sinonasal epithelial cells in chronic rhinosinusitis. Cytoskeleton (Hoboken). 2017; 74: 82-90. [Crossref]
20. Bai J, Tan BK, Kato A. Endotypic heterogeneity and pathogenesis in chronic rhinosinusitis. Curr Opin Allergy Clin Immunol. 2024; 24: 1-8. [Crossref]
21. Shi LL, Xiong P, Zhang L, Cao PP, Liao B, Lu X, et al. Features of airway remodeling in different types of Chinese chronic rhinosinusitis are associated with inflammation patterns. Allergy. 2013; 68: 101-9. [Crossref]
22. Gillesberg FS, Pehrsson M, Bay-Jensen AC, Frederiksen P, Karsdal M, Deleuran BW, et al. Regulation of fibronectin and collagens type I, III and VI by TNF-α, TGF-β, IL-13, and tofacitinib. Sci Rep. 2025; 15: 1087. [Crossref]