A prospective cohort study comparing the effects of different middle turbinate treatments on olfactory function recovery in CRSwNP patients after FESS

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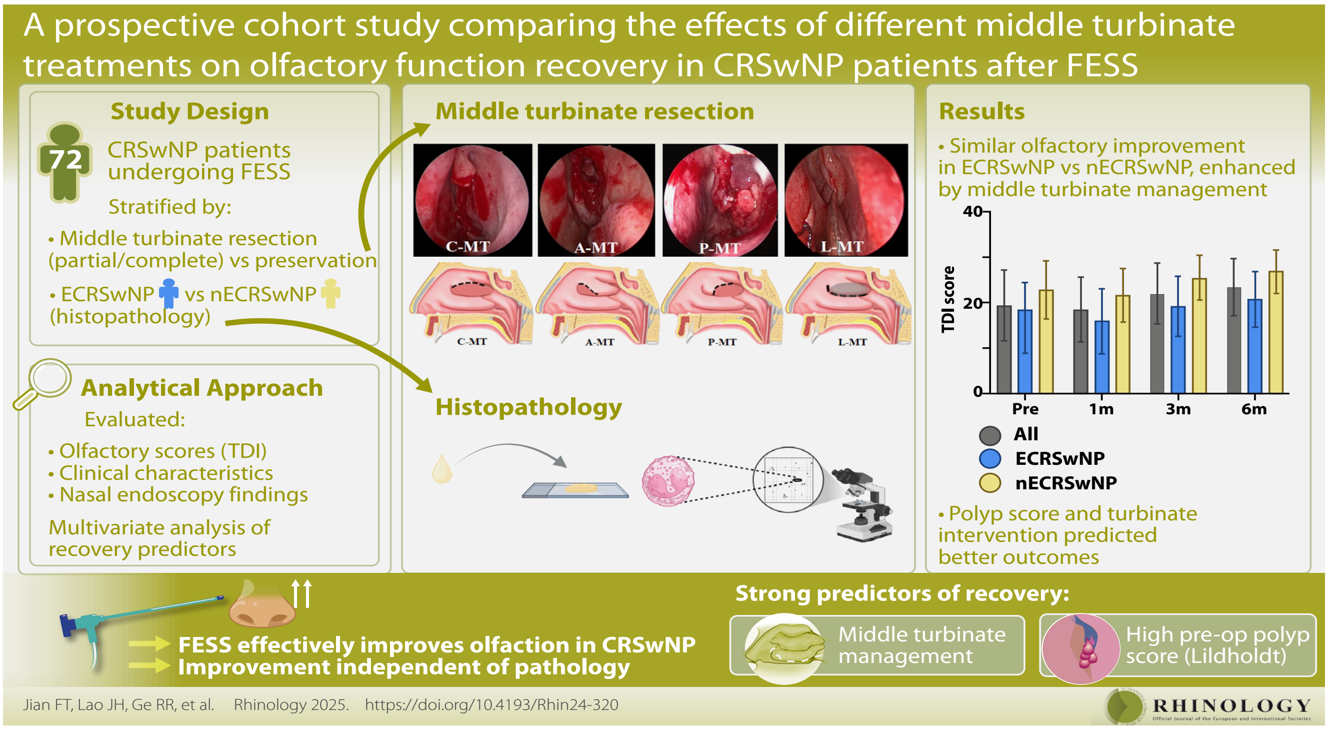

Abstract

Background: The factors affecting postoperative olfactory recovery in chronic rhinosinusitis with nasal polyps (CRSwNP) remain unclear. This study explores postoperative pathological classification and the impact of different middle turbinate management strategies on olfactory recovery. **Methodology**: Seventy-two CRSwNP patients undergoing functional endoscopic sinus surgery (FESS) with ≥6 months follow-up were classified into eosinophilic (ECRSwNP) and non-eosinophilic (nECRSwNP) groups. Based on middle turbinate management, patients were further divided into resection (partial/complete) and preservation groups. Olfactory scores, clinical characteristics, and nasal endoscopy findings were analyzed, and multifactorial analysis identified factors influencing olfactory recovery. **Results**: TDI scores in the ECRSwNP group remained lower than those in the nECRSwNP group preoperatively and postoperatively. However, olfactory score improvement and the proportion of significantly improved patients did not differ significantly between the two groups. Middle turbinate management was associated with greater olfactory improvement, particularly in nECRSwNP patients. Although the complete middle turbinate resection group had lower preoperative olfactory scores than the partial resection group, no significant difference was observed in postoperative olfactory improvement between the two approaches.Higher preoperative polyp scores and middle turbinate management predicted olfactory improvement. **Conclusions**: FESS significantly improves the olfactory function in CRSwNP patients, and the extent of olfactory improvement is independent of pathological type. Patients with higher preoperative Lildholdt polyp scores and those who underwent middle turbinate management during FESS were more likely to exhibit improved olfactory function at 6 months postoperatively.

Key words: middle turbinate, olfaction, EPOS 2020, chronic rhinosinusitis with nasal polyps

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) significantly impacts patients' quality of life, especially their olfactory function [1-2]. Although functional endoscopic sinus surgery (FESS) is the primary treatment, the factors influencing postoperative olfactory recovery remain unclear [3-4]. Despite numerous reviews and meta-analyses in recent years, the influence of surgical intervention versus the pathological subtypes of CRSwNP on postoperative olfactory recovery remains unclear [5]. Particularly, the handling of the middle turbinate in FESS has been a focal point among rhinologists [6].

Together, the middle turbinate and superior turbinate together form the lateral boundary of the olfactory cleft. The shape of the middle turbinate plays an important role in separating and guiding airflow into the olfactory cleft, contributing to the protection of the olfactory region from external stimuli, warming and humidifying the air, and maintaining a stable airflow in the olfactory cleft [7]. However, in FESS, the proper management of the middle turbinate remains a subject of debate, with arguments both for and against its removal. In 2000, Leopold et al. [8] studied the distribution of olfactory neurons through immunohistochemistry and electroencephalography and found that olfactory nerve fibers extend along the medial surface of the middle turbinate to its anterior portion. Theoretically, removing these receptors could impair olfactory function. Therefore, opponents of middle turbinate resection argue that its removal would reduce the number of olfactory neurons, disrupt the anatomical structure of the olfactory cleft, alter airflow dynamics, and hinder the interaction between odorant molecules and olfactory neurons, thereby negatively affecting olfactory function [6,9-12]. On the other hand, proponents of middle turbinate resection suggest that in CRSwNP patients with anatomical abnormalities of the middle turbinate (such as concha bullosa or paradoxical turbinate) or polypoid changes may lead to airway obstruction, reducing the chances of odorant molecules reaching the olfactory cleft. Appropriate resection of the middle turbinate could improve nasal airflow, allowing odorant molecules to more easily reach the olfactory cleft, thus improving olfactory function [13-16]. Additionally, some researchers have proposed that this improvement is not only due to widening the passage for odorant molecules but also related to the removal of polypoid tissue filled with inflammatory cells and mediators, which reduces the inflammatory load and thereby enhances olfactory function [4,17-18]. These differing perspectives have led to various surgical approaches to the middle turbinate in FESS, making the optimization of middle turbinate surgical techniques to enhance postoperative olfactory recovery a focal point of debate among rhinology experts.

Therefore, although there is controversy regarding whether the middle turbinate should be removed during FESS, its potential in improving postoperative olfactory recovery remains a key issue in current research and practice. To further explore this topic, this study meticulously analyzes the changes in olfaction in CRSwNP patients with different pathological subtypes, comparing the middle turbinate resection group and non-resection group preoperatively and at 6 months postoperatively. The study aims to reveal the various factors influencing postoperative olfactory recovery, including patients' baseline clinical characteristics, postoperative pathological subtypes, the severity of nasal polyps, and the management of the middle turbinate during surgery.

Materials and methods

Study design

This prospective cohort study enrolled 72 patients with CRSwNP who underwent FESS from March 2023 to December 2023. Follow-ups were conducted at 1-, 3-, and 6-months post-surgery. Preoperative general information, nasal endoscopy and imaging results, and olfactory changes within 6 months post-surgery were collected. Patients were categorized into two groups based on postoperative pathology: ECRSwNP and nECRSwNP. Additionally, they were divided into two subgroups based on the treatment of the middle turbinate during FESS: middle turbinate resection and middle turbinate preservation. This study was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University (II2023-056-01). Written informed consent was obtained from all patients.

Participants

All patients were diagnosed with CRSwNP according to the EPOS-2020 diagnostic criteria and underwent EFSS surgery under general anesthesia, with the extent of surgery adjusted according to the severity of their condition. Postoperative care included nasal spray with mometasone furoate and nasal saline irrigation. The follow-up duration was more than 6 months; patients were aged >18 years. According to the 2010 Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, the diagnosis of allergic rhinitis is made based on the patient's typical clinical symptoms (nasal itching, sneezing, rhinorrhea, and nasal congestion, as well as ocular symptoms), physical examination findings (pale, edematous nasal mucosa and clear, watery nasal discharge), and positive results from skin prick tests (SPT) or serum-specific IgE testsing [19]. According to the 2014 Global Initiative for Asthma (GINA) guidelines, asthma is diagnosed based on a comprehensive assessment of the patient's medical history (recurrent episodes of wheezing, shortness of breath, chest tightness, or coughing), clinical signs (scattered or diffuse wheezing sounds in both lungs during attacks), and pulmonary function tests (positive bronchial provocation test or bronchodilator test, with a diurnal variability of peak expiratory flow (PEF) of 20% or greater). The diagnosis is made by a respiratory specialist [20]. None of the patients had taken oral corticosteroids,

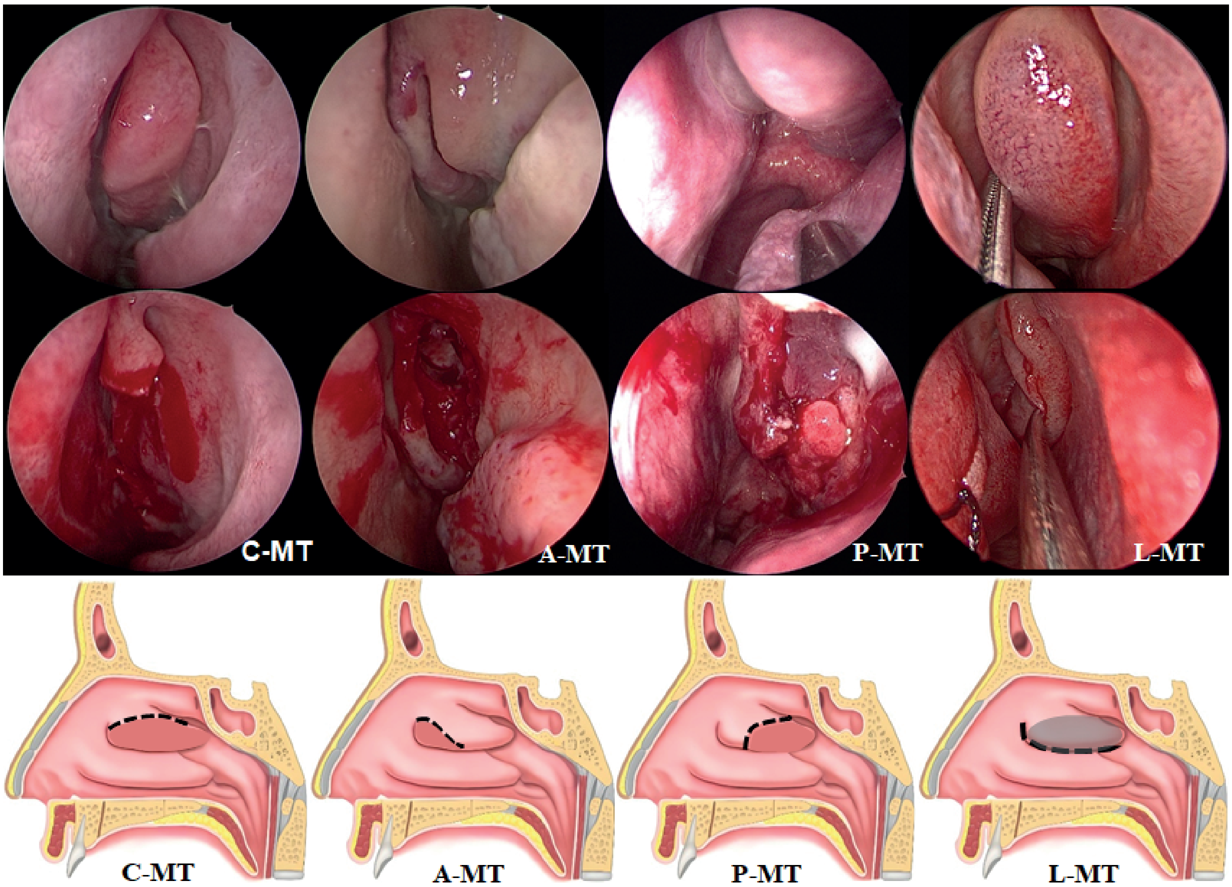

Figure 1. The first line: Preoperative; The second line: Types of middle turbinate resection intraoperatively; Third line: Schematic diagram of the type of middle turbinate resection. C-MT: complete middle turbinate of the bulb resection; A-MT: anterior 1/3 middle turbinate resection; P-MT: posterior middle turbinate resection; L-MT: lateral middle turbinate resection. Black dashed line: cut edge; Dark pink part: excision range; Grey shade: Mucosa retained, middle turbinate bone area removed.

antibiotics, or biologics within one month prior to surgery. Postoperatively, none of the patients used oral corticosteroids, and they were only given mometasone furoate nasal spray and saline irrigation. Exclusion criteria included fungal sinusitis, cystic fibrosis, inverted papilloma, eosinophilic granulomatosis with polyangiitis, incomplete data, pregnancy, lactation, and active COVID-19 infection or recent contact with COVID-19 patients.

Variables and measurements

Visual Analogue Scale (VAS)

A 10-point Visual Analogue Scale (VAS) was used to assess patients' subjective symptoms. This scale evaluates the severity of overall nasal symptoms and their impact on daily life, including nasal congestion, rhinorrhea, headache, and olfactory dysfunction. One item in the VAS specifically addresses olfactory dysfunction, which was used in this study for subjective evaluation of smell. The VAS scores range from 0-3 points(mild), 4-6 points (moderate), and 7-10 points (severe), with scores above 5 indicating a significant impact on daily life [21].

Assessment of Quality of Life

The Sino-Nasal Outcome Test (SNOT-22) questionnaire is used to measure sinonasal symptoms and assess the quality of life in patients [22]. This questionnaire consists of 22 items, each scored from 0 to 5, with 0 indicating no impact and 5 indicating a severe impact. The total score, summing all item scores, ranges up to 110.

Lund-Kennedy Score

Nasal mucosa was assessed endoscopically for the presence of polyps, edema, secretions, scarring, and crusting, with separate scores for the left and right sides. Scoring criteria were as follows: Polyps: 0 = none, 1 = in the middle meatus, 2 = beyond the middle meatus.Edema: 0 = none, 1 = mild, 2 = severe;Secretions: 0 = none, 1 = clear and thin, 2 = thick and purulent; Scarring: 0 = none, 1 = mild, 2 = severe (only for surgical outcome evaluation);Crusting: 0 = none, 1 = mild, 2 = severe (only for surgical outcome evaluation); Each side scored 0-10, with a total score of 0-20.

Table 1. Patient's baseline clinical characteristics [1].

Parameters	ECRSwNP (n=40)	nECRSwNP (n=32)	All (n=72)	P
Sex				0.692
Male	28 (70.00%)	21 (65.63%)	49 (68.06%)	
Female	12 (30.00%)	11 (34.38%)	23 (31.94%)	
Age, year	44.33±11.27	39.34±15.19	42.11±13.29	0.115
BMI, kg/m²	24.37±2.38	22.63±3.74	23.60±3.16	0.019*
Disease course, month	38.68±64.94	13.72±21.83	27.58±51.77	0.027*
Family disease history	7 (17.50%)	4 (12.50%)	11 (15.28%)	0.744
No	33 (82.50%)	28 (87.50%)	61 (84.72%)	0.301
AR	5 (12.50%)	4 (12.50%)	9 (12.50%)	
Sinusitis	2 (5.00%)	0	2 (2.78%)	
Allergy history	25 (62.50%)	5 (15.63%)	30 (41.67%)	<0.001*
No	15 (37.50%)	27 (84.38%)	42 (58.33%)	<0.001*
AR	14 (35.00%)	4 (12.50%)	18 (25.00%)	
Asthma	1 (2.50%)	1 (3.13%)	2 (2.78%)	
AR+Asthma	10 (25.00%)	0	10 (13.89%)	
Smoking				0.949
No	31 (77.50%)	25 (78.13%)	56 (77.78%)	
Yes	9 (22.50%)	7 (21.88%)	16 (22.22%)	
Nasal surgery history				0.273
No	32 (80.00%)	22 (68.75%)	54 (75.00%)	
Yes	8 (20.00%)	10 (31.25%)	18 (25.00%)	
Pre-treatment				
Symptom VAS	25.30±12.74	21.69±12.32	23.69±12.60	0.229
Olfactory VAS	6.65±3.45	3.78±3.49	5.38±3.73	<0.001*
SNOT-22	33.98±19.09	33.28±20.24	33.67±19.48	0.882
Lund-Mackay score	15.83±4.37	15.59±4.61	15.72±4.45	0.828
Olfactory cleft score	1.20±1.80	0.19±0.78	0.75±1.52	0.002*
Lund - Kennedy score	10.18±3.04	9.91±2.28	10.06±2.71	0.679
IgE	246.45±309.93	159.66±303.41	207.88±307.97	0.237
bNEU, %	0.59±0.14	0.56±0.10	0.58±0.12	0.257
bLY, %	0.30±0.10	0.32±0.10	0.31±0.10	0.257
bEOS, %	0.04±0.03	0.05±0.12	0.05±0.08	0.887
Lildholdt polyp score	3.80±1.24	3.38±1.60	3.61±1.42	0.209

Note: *, $p < 0.05$; ECRSwNP, Eosinophilic chronic rhinosinusitis with nasal polyps; nECRSwNP, non-eosinophilic chronic rhinosinusitis with nasal polyps; bNEU, peripheral blood neutrophils; bLY, peripheral blood lymphocyte; bEOS, Peripheral blood eosinophils.

Polyp score

A senior rhinologist used nasal endoscopy and the Lildholdt classification method [23,24] to score the polyps on each side. The scores were as follows: 0 = no nasal polyps, 1 = polyps not reaching the upper edge of the inferior turbinate, 2 = polyps between the upper and lower edges of the inferior turbinate, 3 = polyps reaching the lower edge of the inferior turbinate. The total score (sum of both sides) ranges from 0 to 6, with 1-2 as mild, 3-4 as moderate, and 5-6 as severe.

Lund-Mackay score of sinus CT

Six regions are scored: maxillary sinus, anterior ethmoid sinus, posterior ethmoid sinus, sphenoid sinus, frontal sinus, and osteomeatal complex (OMC). The scoring criteria are as follow: Sinuses: 0 = normal, 1 = partial shadowing (mucosal thickening), 2 = complete.shadowing (or highly shadowing), OMC: 0 = no obstruction, 2 = obstruction. Each side scored 0-12, with a total score ranging from 0-24. Separately, the olfactory cleft area was scored, with unilateral lesions recorded as 0 and 2 points: 0 = no

Table 2. Patient's baseline clinical characteristics [2].

Parameters	Middle turbinate resection		P
	No (n=23)	Yes (n=49)	
Symptom VAS	25.39±11.45	22.90±13.14	0.437
SNOT-22	33.00±22.67	34.00±18.03	0.844
Lund-Mackay score	14.74±4.47	15.98±4.55	0.282
TDI score (Pre)	20.30±5.37	18.88±8.75	0.398

Note: * p < 0.05

Table 3. Changes in postoperative olfactory TDI scores.

Parameters	ECRSwNP (n=40)	nECRSwNP (n=32)	All (n=72)	P
Middle turbinate resection				0.692
No	12 (30.00%)	11 (34.38%)	23 (31.94%)	
Yes	28 (70.00%)	21 (65.63%)	49 (68.06%)	
TDI score				
Pre	16.56±7.79	22.80±6.43	19.33±7.82	<0.001*
1 month	15.88±7.15	21.59±5.88	18.41±7.16	<0.001*
3 month	19.16±6.61	25.48±4.93	21.97±6.68	<0.001*
6 month	20.66±6.09	26.82±4.75	23.39±6.30	<0.001*
Change between pre and 6m	4.09±5.75	4.02±3.76	4.06±4.94	0.949
Olfactory stage (pre)				0.046*
Normosmia	3 (7.50%)	2 (6.25%)	5 (6.94%)	
Hyposmia	19 (47.50%)	24 (75.00%)	43 (59.72%)	
Anosmia	18 (45.00%)	6 (18.75%)	24 (33.33%)	
Olfactory stage (6 month)				0.005*
Normosmia	1 (2.50%)	5 (15.63%)	6 (8.33%)	
Hyposmia	29 (72.50%)	26 (81.25%)	55 (76.39%)	
Anosmia	10 (25.00%)	1 (3.13%)	11 (15.28%)	
Olfactory improving ≥ 5.5 score at 6 month				0.502
No	28 (70.00%)	20 (62.50%)	48 (66.67%)	
Yes	12 (30.00%)	12 (37.50%)	24 (33.33%)	

Note: * p < 0.05.

obstruction, 2 = obstruction.

Olfactory testing
Olfactory testing using Sniffin' Sticks (Burghart, Germany) was conducted 1 day before surgery and at 1-, 3-, and 6-months post-surgery. The test includes odor threshold, discrimination, and identification subtests, with a total TDI score ranging from 1 to 48. Scores were categorized as normosmia (TDI > 30.5), hyposmia (16.5-30.5), and functional anosmia (< 16.5). A TDI score improvement of ≥5.5 was considered significant improvement [25].

Histological assessment
Tissue samples of polyps were collected during surgery for hematoxylin-eosin (HE) staining. A pathologist examined the samples under a 400× microscope and recorded observations from ten randomly selected fields of view. The diagnostic threshold was set at tEOS ≥10/HPF, classifying patients into two groups: ECRSwNP and nECRSwNP [4].

Middle turbinate management
All surgeries were performed by the same senior rhinologist. The principle for managing the middle turbinate during surgery was to preserve the middle turbinate as much as possible and

Table 4. The impact of different middle turbinate management methods on postoperative olfactory function recovery.

	Middle turbinate resection			
	No	Yes	All	P
All patients				
Sample size (n)	23	49	72	
TDI score				
Pre	20.30±5.37	18.88±8.75	19.33±7.82	0.474
1 month	18.80±4.79	18.23±8.08	18.41±7.16	0.753
3 month	21.90±5.47	21.99±7.23	21.97±6.68	0.957
6 month	22.43±5.44	23.85±6.68	23.39±6.30	0.377
Change between pre and 6m	2.12±2.49	4.97±5.53	4.06±4.94	0.021*
TDI stage (pre)				0.028*
Normal	0	5 (10.20%)	5 (6.94%)	
Hyposmia	18 (78.26%)	25 (51.02%)	43 (59.72%)	
Anosmia	5 (21.74%)	19 (38.78%)	24 (33.33%)	
TDI stage (6 month)				0.087
Normal	0	6 (12.24%)	6 (8.33%)	
Hyposmia	19 (82.61%)	36 (73.47%)	55 (76.39%)	
Anosmia	4 (17.39%)	7 (14.29%)	11 (15.28%)	
TDI improving ≥ 5.5 score at 6 month				0.002*
No	21 (91.30%)	27 (55.10%)	48 (66.67%)	
Yes	2 (8.70%)	22 (44.90%)	24 (33.33%)	
ECRSwNP group				
Sample size (n)	12	28	40	
TDI				
Pre	17.58±4.87	16.13±8.80	16.56±7.79	0.594
1 month	17.04±5.18	15.38±7.87	15.88±7.15	0.506
3 month	19.00±5.36	19.22±7.17	19.16±6.61	0.924
6 month	19.44±4.83	21.18±6.57	20.66±6.09	0.414
Change between pre and 6m	1.85±2.61	5.05±6.47	4.09±5.75	0.108
TDI stage (pre)				0.140
Normal	0	3 (10.71%)	3 (7.50%)	
Hyposmia	8 (66.67%)	11 (39.29%)	19 (47.50%)	
Anosmia	4 (33.33%)	14 (50.00%)	18 (45.00%)	
TDI stage (6 month)				0.536
Normal	0	1 (3.57%)	1 (2.50%)	
Hyposmia	8 (66.67%)	21 (75.00%)	29 (72.50%)	
Anosmia	4 (33.33%)	6 (21.43%)	10 (25.00%)	
TDI improving ≥ 5.5 score at 6 month				0.067
No	11 (91.67%)	17 (60.71%)	28 (70.00%)	
Yes	1 (8.33%)	11 (39.29%)	12 (30.00%)	
nECRSwNP group				
Sample size (n)	11	21	32	
TDI				
Pre	23.27±4.34	22.55±7.39	22.80±6.43	0.767
1 month	20.73±3.62	22.04±6.81	21.59±5.88	0.559
3 month	25.07±3.61	25.69±5.57	25.48±4.93	0.741

Table 4 *continued*. The impact of different middle turbinate management methods on postoperative olfactory function recovery.

	Middle turbinate resection			
	No	Yes	All	P
6 month	25.69±4.11	27.40±5.05	26.82±4.75	0.340
Change between pre and 6m	2.42±2.44	4.86±4.10	4.02±3.76	0.081
TDI stage (pre)				0.204
Normal	0	2 (9.52%)	2 (6.25%)	
Hyposmia	10 (90.91%)	14 (66.67%)	24 (75.00%)	
Anosmia	1 (9.09%)	5 (23.81%)	6 (18.75%)	
TDI stage (6 month)				0.056
Normal	0	5 (23.81%)	5 (15.63%)	
Hyposmia	11 (100.00%)	15 (71.43%)	26 (81.25%)	
Anosmia	0	1 (4.76%)	1 (3.13%)	
TDI improving ≥ 5.5 score at 6 month				0.023*
No	10 (90.91%)	10 (47.62%)	20 (62.50%)	
Yes	1 (9.09%)	11 (52.38%)	12 (37.50%)	

Note: * $p < 0.05$

avoid excessive resection. Middle turbinate resection was only considered in the following three situations [4]: 1) Hypertrophy of the middle turbinate causes ventilation obstruction or blocks the sinus openings, impairing surgical outcomes; 2) The middle turbinate cannot be restored to its normal function, potentially affecting ciliary activity and nasal clearance; 3) The patient has severe polypoid changes or other anatomical abnormalities originating from the middle turbinate, which affect the overall surgical outcomes.

The extent of middle turbinate resection was categorized as follows: anterior 1/3 middle turbinate resection (A-MT); complete middle turbinate resection (C-MT); lateral middle turbinate resection (L-MT); posterior middle turbinate resection (P-MT). For concha bullosa, paradoxical middle turbinate, and turbinate bone thickening, the L-MT resection method was generally employed, removing the lateral mucosa and the lateral bone of the concha bullosa. For anterior turbinate polyps or lesions causing obstruction of the anterior group sinus ostia, the A-MT resection method was typically applied, removing the anterior 1/3 of the middle turbinate bone and mucosa. For polyps or lesions originating from the posterior part of the middle turbinate causing obstruction of the posterior group ethmoid and sphenoid sinus ostia, the P-MT resection method was generally adopted, removing the posterior part of the middle turbinate bone and mucosa. For overall polypoid changes of the middle turbinate, where the turbinate bone is almost compressed and resorbed irreversibly, the C-MT resection method was typically used to remove the entire middle turbinate bone and mucosa. In other cases, every effort was made to preserve the integrity of the middle turbinate mucosa and bone. Details of the resection extents are shown in Figure 1.

Statistical analysis

Continuous variables were reported with mean and standard deviation (SD). Group comparisons were made using Student's independent t-test. One-way ANOVA and Fisher's LSD post-hoc comparisons were used for mean comparisons among four ypes of middle turbinate resection. To avoid the inflation of Type I error, post-hoc comparisons between paired groups are only conducted when the overall ANOVA is significant. Categorical variables were presented as numbers and percentages and compared using the Chi-square test or Fisher's exact test (if the expected value ≤ 5). One-way repeated measures ANOVA (rANOVA) was used to check the linear trend of TDI scores from pre-treatment to the sixth month post-treatment; If the linear contrast is significant, it indicates that the numerical changes exhibit an increasing or decreasing trend over time. Univariate and multivariate logistic regression models were used to investigate the independent variables associated with postoperative improvement of TDI score. The multivariate model used a forward method and the Wald test to select the best combination of associated factors from all independent variables. To avoid multicollinearity, correlation analysis (including Pearson's r and Spearman's rho) will be used to check whether variables selected for the multivariable model have high correlations (r or rho > 0.80) with each other. Only one of the highly correlated variables will be retained in the model. ROC analysis was used to check the diagnostic efficacy of the final multivariate model.

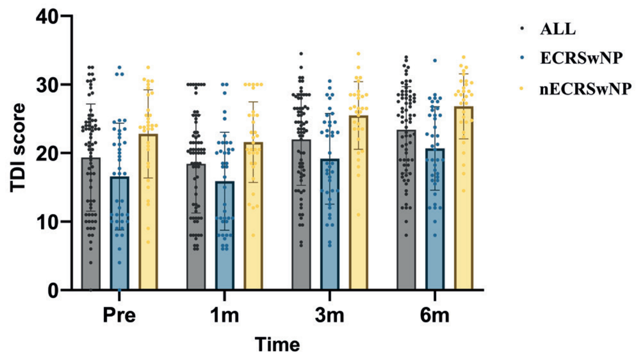

Figure 2. Olfactory improvement in different groups after surgery.

The statistical significance for all tests was set at a p-value < 0.05 (two-tailed). The diagnostic effectiveness of the multivariate model was checked by ROC analysis using the 'pROC' package. All analyses were performed using IBM SPSS Version 25.

Results

Comparison of clinical baseline characteristics

A total of 72 patients with CRSwNP were enrolled in this study (49 males, 23 females; age range 18-69 years, mean age 42.11 ± 13.29 years). Among them, 49 patients (68.06%) partial or complete middle turbinate resection, while 23 patients (31.94%) had preservation of the middle turbinate. The A-MT group had 13 individuals; the C-MT group had 17 individuals; the L-MT group had 11 individuals; and the P-MT group had 8 individuals. There were 40 cases (55.56%) of ECRSwNP and 32 cases (44.44%) of nECRSwNP. Patients in the ECRSwNP group had a significantly higher body mass index (BMI), longer disease duration,a higher proportion of allergy history, and higher olfactory VAS and olfactory cleft scores (all P < 0.05). Other baseline characteristics are shown in Table 1. There were no significant differences in the preoperative disease severity between the middle turbinate resection group and the non-resection group, whether assessed by the subjective VAS and SNOT-22 scores or the objective Lund-Mackay score based on CT scans. Additionally, there were no significant differences in the preoperative olfactory TDI scores between the two groups, with P values all > 0.05. Baseline characteristics are shown in Table 2.

Changes in postoperative olfactory TDIs scores

To analyze the changes in olfactory function after FESS, we obtained TDI scores for 72 patients at preoperative, 1 month, 3 months, and 6 months postoperative intervals. Preoperatively, 5 patients (6.94%) had normal olfaction, 43 patients (59.72%) had hyposmia, and 24 patients (33.33%) had functional anosmia. At 6 months after surgery, 6 patients (8.33%) had normal olfaction, 55 patients (76.39%) had hyposmia, and 11 patients (15.28%) had anosmia. The average increase in TDI scores at 6 months postoperative was 4.06 points. Regarding the MCID for the Sniffin' Sticks TDI score, approximately one-third (n=24) of the participants improved by 5.5 points or more. Fourteen patients showed an improvement in olfaction (from hyposmia to normosmia or from anosmia to hyposmia or normosmia). Of these, in the ECRS group, 8 cases of anosmia changed to hyposmia, and 2 cases of normosmia changed to hyposmia. In the nECRSwNP group, 8 patients' olfaction changed from anosmia to hyposmia. Table 3 provides information on the changes in TDI from pre-treatment to the sixth month after treatment. The results reveal that the TDI in the ECRSwNP group was significantly lower than that in the nECRSwNP group from preoperative to the sixth month postoperative (all P<0.001). However, when looking at the change in scores after adjusting for baseline, the increase in scores between the two groups was not significantly different (P=0.949). Similarly, when viewed by stage, although the proportion of people with better status in the nECRSwNP group was higher than that in the ECRSwNP group at baseline and the sixth month, there was no significant difference in the proportion of those who improved by more than 5.5 points after six months (P=0.502). Figure 2 shows the linear trends of the patients. In the enture cohort of patients and within each ECRSwNP group, the gradually ascending trend of TDI passed the significance test of linear trends (all P<0.001). Interestingly, we observed a decline in TDI scores within the first month postoperatively, followed by an improvement in olfactory scores thereafter.

The impact of different middle turbinate management methods on postoperative olfactory function recovery

To validate the impact of middle turbinate resection on patients TDI scores, verification was carried out in three sub-samples: the entire patient cohort, the ECRSwNP group, and the nECRSwNP group. The results (Table 4 and Figure 2) indicated that there were no significant differences in the raw TDI scores among those groups at four time points. However, patients who underwent middle turbinate resection showed significantly higher mean improvement scores in TDI than those who did not, both in the average improvement score of the entire patient cohort (P=0.021) and in the number of patients in the entire cohort (P=0.002) and the nECRSwNP group (P=0.023) who met the improvement criteria after six months (Table 4 and Figure 3). Patients who underwent middle turbinate resection were divided into four types: A-MT, C-MT, L-MT, and P-MT. The degree of improvement in TDI among the four types was also compared. As indicated in Table 5, the change in TDI at six months post-operation did not show significant differences among the four types of resection, including omnibus one-way ANOVA and all pairwise post-hoc comparisons (all P>0.05).Additionally, we compared the baseline characteristics and postoperative olfactory outcomes between partial middle turbinate resection

Table 5. The impact of different types of nasal turbinate surgery on olfactory function recovery.

Data set	Middle turbinate resection type				F	P
	A-MT (n=13)	C-MT (n=17)	L-MT (n=11)	P-MT (n=8)		
All patients	5.77±5.03	4.22±4.66	5.20±7.31	4.94±6.12	0.19	0.902
ECRSwNP	5.71±5.99	4.19±4.19	7.75±11.79	4.00±8.96	0.34	0.796
nECRSwNP	5.83±4.21	4.31±6.75	3.75±3.59	5.88±2.17	0.35	0.789

Note: * p < 0.05

Table 6. The impact of partial vs. complete middle turbinate resection on postoperative olfactory recovery.

Parameters	Middle turbinate resection		P
	partial (n=32)	complete (n=17)	
Symptom VAS	18.97±12.37	30.29±11.51	0.003 *
SNOT-22	31.88±17.67	37.94±18.57	0.267
Lund-Mackay score	15.66±4.68	17.18±3.78	0.255
TDI score(Pre)	20.79±9.10	15.27±6.93	0.034 *
TDI score(1 month)	21.04±7.38	12.94±6.7	0001*
TDI score(3 month)	24.23±6.19	17.79±7.35	0.002*
TDI score(6 month)	26.16±5.67	19.50±6.38	0.001 *
Change between pre and 6m	5.58±5.75	4.72±4.12	0.586
TDI improving ≥ 5.5 score at 6 month			
N0	16 (50.00%)	11 (64.71%)	
Yes	16 (50.00%)	6 (35.29%)	0.325

Note: * p < 0.05

(A-MT, L-MT, and P-MT) and complete middle turbinate resection (C-MT). Although the preoperative subjective VAS scores and olfactory TDI scores in the complete resection (C-MT) group differed significantly from those in the partial resection (A-MT, L-MT, P-MT) group (all P < 0.05), no significant differences were observed in the changes in TDI scores or the proportion of patients with significant olfactory improvement at 6 months postoperatively between the two groups (P > 0.05). See Table 6 for details.

Analysis of factors associated with postoperative olfactory improvement

We found that patients with higher Lund-Mackay scores (OR=1.15), higher polyp score (OR=1.77), and those who underwent middle turbinate resection (OR=8.56) were more likely to improve their TDI scores after 6 months. However, a higher level of pre-treatment TDI score (OR=0.90) seems to have a lower opportunity for improving TDI (Table 7). After selection by the multivariate model, two factors were chosen: Lildholdt polyp score and middle turbinate resection. As shown, patients with higher Lildholdt polyp score (OR=1.90) and those undergoing middle turbinate resection (OR=10.66) were more likely to improve TDI scores after six months (both P=0.005). This is the final multivariate model. The ROC analysis of this final multivariate model indicates good diagnostic efficacy in predicting the improvement of TDI after six months (AUC=0.809). The sensitivity and specificity were 0.71 and 0.81, respectively (Figure 4).

Discussion

Olfactory dysfunction is one of the most challenging symptoms to treat in patients with CRSwNP (26). Most scholars agree that FESS can effectively improve olfactory dysfunction in CRSwNP patients [5,23,26-29]. Similarly, our study found that the average TDI score increased by 4.06 points at six months after FESS, with one-third of the patients showing significant improvement (TDI > 5.5 points). Among them, 30% of patients in the ECRSwNP group and 37.5% in the nECRSwNP group (TDI > 5.5 points) showed significant olfactory improvement. This improvement in olfaction may be due to the surgical removal of nasal polyps, which eliminated obstructive factors in the nasal cavity, improved airflow, and thereby enhanced olfactory function. Although the rate of complete recovery of olfactory function postoperatively was not high, the proportion of patients with different levels of olfactory function changed significantly. More than

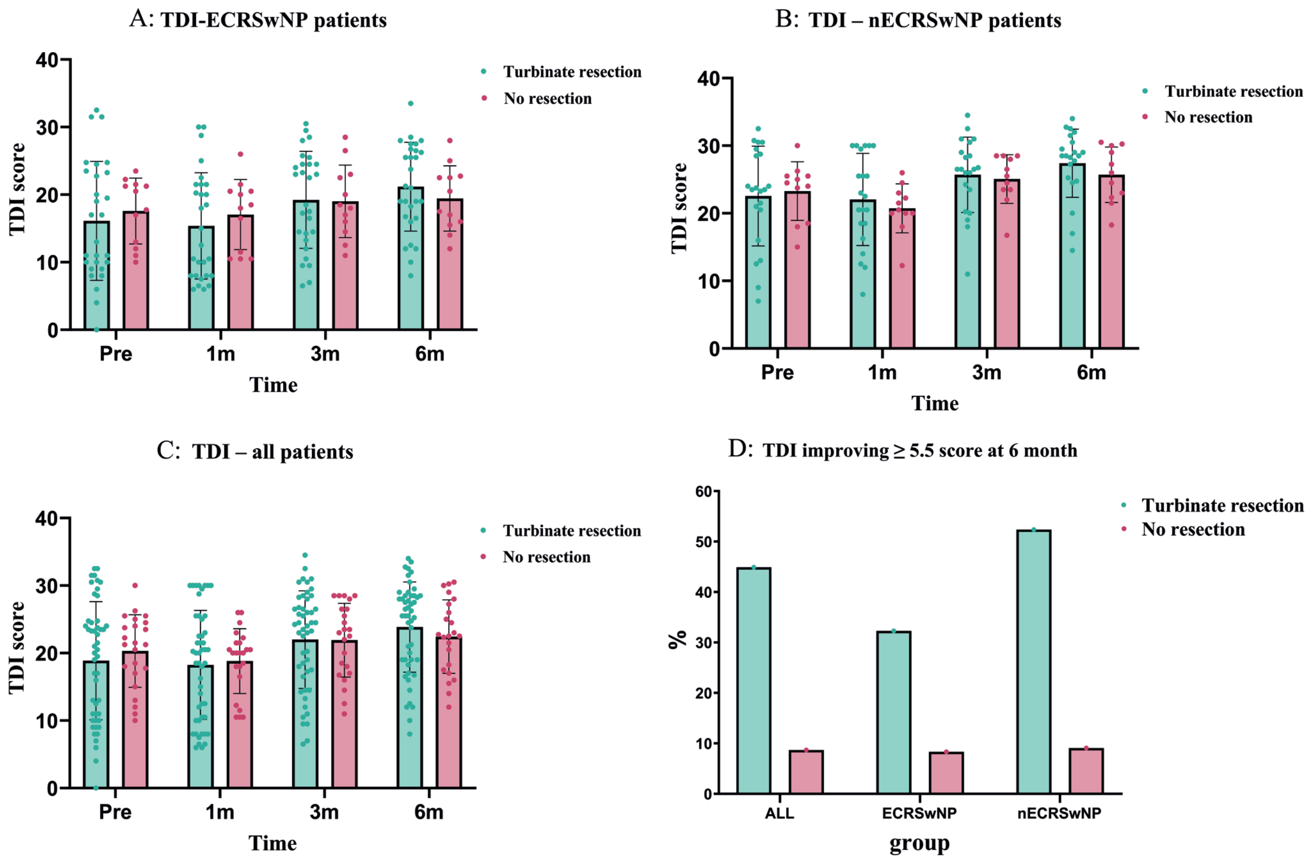

Figure 3. Postoperative TDI score improvement with different middle turbinate treatments and the number of people with significant olfactory improvement at 6 months after surgery.

18% of patients transitioned from anosmia to hyposmia, indicating that FESS surgery has a more pronounced effect on patients with anosmia compared to those with better olfactory function. Additionally, univariate analysis revealed that a higher preoperative TDI score (OR = 0.90) was associated with a lower chance of postoperative olfactory improvement. This is consistent with previous research findings [12,26].

In this study, we evaluated the olfactory recovery of CRSwNP patients from preoperative to six months postoperative after FESS. We found that, both at baseline and six months after surgery, the olfactory scores of the nECRSwNP group were higher than those of the ECRSwNP group, consistent with previous studies showing that patients with ECRSwNP, which is characterized by type II inflammation, experience more severe olfactory loss [26,27].

In the ECRSwNP group, 2 patients experienced worsening olfactory function. Neither of these patients underwent middle turbinate resection, so it is unlikely that the decrease in olfactory function was caused by the middle turbinate surgery. This may be related to the longer recovery time for patients in the ECRS group and the recurrent type II inflammation during the postoperative recovery process, leading to mucosal edema in the olfactory cleft. However, we found no statistically significant difference in the increase of olfactory scores between the ECRSwNP and nECRSwNP groups six months postoperatively when compared to baseline. The proportion of patients with significant olfactory improvement also did not differ significantly between the two groups six months after surgery. We concluded that pathological typing may not be the main factor influencing postoperative olfactory improvement.

Therefore, we conducted a multivariate analysis to establish a multifactorial predictive model for postoperative olfactory recovery. We found that the severity of nasal polyps and middle turbinate resection during surgery had a significant impact on postoperative olfactory recovery in CRSwNP patients. This study used the Lildholdt score to distinguish the severity of nasal polyps. Like the study of Haxel [23] et al., we found that a higher Lildholdt polyp score is associated with better postoperative olfactory recovery. The severity of preoperative polyps is positively correlated with the improvement in postoperative olfactory scores [5,27-29].

Meanwhile, our study also focused on the impact of middle turbinate resection during FESS on postoperative olfactory recovery. We verified this in three sub-samples: the overall patient cohort, the ECRSwNP group, and the nECRSwNP group. The results showed that six months postoperatively, both the increase in TDI scores and the number of patients with signifi-

Table 7. Univariate logistic regression results for postoperative olfactory function improvement.

Parameters	Crude OR (95% CI)	P
Sex		
Male	1	-
Female	1.92 (0.69 to 5.39)	0.214
Age, year	0.98 (0.95 to 1.02)	0.410
BMI, kg/m^2	0.91 (0.77 to 1.07)	0.234
Disease course, month	1.00 (0.99 to 1.01)	0.915
Family disease history		
No	1	-
Yes	0.39 (0.08 to 1.99)	0.259
Allergy history		
No	1	-
Yes	0.77 (0.28 to 2.11)	0.612
Smoking		
No	1	-
Yes	0.60 (0.17 to 2.11)	0.426
Nasal surgery history		
No	1	-
Yes	1.39 (0.46 to 4.19)	0.565
Pre-treatment		
Symptom VAS	0.98 (0.94 to 1.02)	0.253
Olfactory VAS	1.11 (0.97 to 1.27)	0.142
SNOT-22	1.00 (0.98 to 1.03)	0.928
Lund-Mackay score	1.15 (1.02 to 1.30)	0.020*
Mackay score	0.95 (0.68 to 1.32)	0.740
Lund- Kennedy score	1.03 (0.86 to 1.24)	0.734
IgE	1.00 (1.00 to 1.00)	0.668
Neutrophil, %	2.15 (0.04 to 113.45)	0.706
Lymphocyte, %	0.22 (0.00 to 29.55)	0.546
EO, %	0.00 (0.00 to 1508.28)	0.242
Lildholdt polyp score	1.77 (1.18 to 2.66)	0.006*
TDI (pre)	0.90 (0.84 to 0.97)	0.005*
Middle turbinate resection		
No	1	-
Yes	8.56 (1.81 to 40.54)	0.007*
Group		
ECRSwNP	1	-
nECRSwNP	1.40 (0.52 to 3.75)	0.503

Note: * $p < 0.05$

cant olfactory improvement were significantly higher in patients who underwent middle turbinate resection compared to those who did not, in the overall patient cohort. This is consistent with the findings of Delarestaghi [30], Marchioni [31], and others, who reported that partial middle turbinate resection during endoscopic sinus surgery can improve olfaction. Regarding the trend of postoperative olfactory improvement, the middle turbinate resection subgroup showed a continuous improvement in olfaction in both pathological subtypes (ECRSwNP and nECRSwNP groups), while the middle turbinate preservation subgroup demonstrated stagnant improvement around 3 months postoperatively (Figures 2A and 2B). We infer that the improvement in olfaction within the first three months post-surgery is primarily due to conductive recovery (removal of nasal polyps). However, the sustained olfactory improvement observed between 3 to 6 months in the middle turbinate resection group may be attributed to middle turbinate resection facilitating the resolution of type II inflammation, leading to both conductive and sensorineural improvement, thus showing a continuous trend in olfactory recovery.

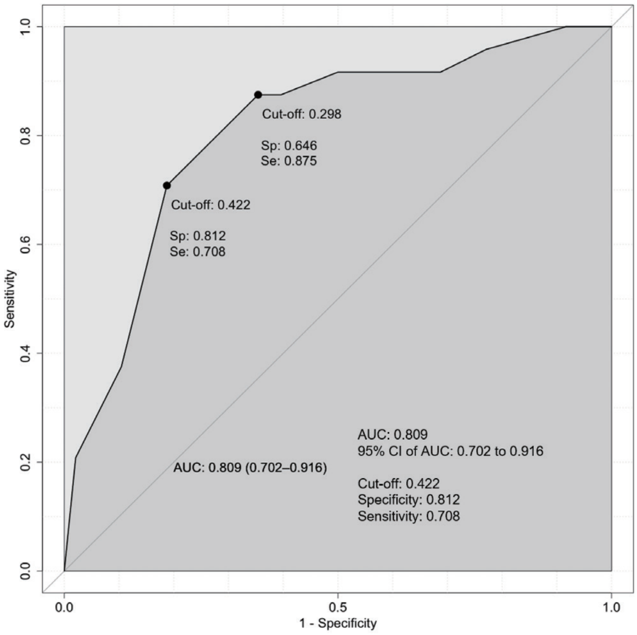

Figure 4. The ROC analysis results of the final multivariate logistic regression model for postoperative olfactory improvement in CRSwNP.

However, within different pathological subgroups, we found that in the nECRSwNP group, the number of patients with significant olfactory improvement was higher in those who underwent middle turbinate resection compared to those who did not. In the ECRSwNP group, there was no statistically significant difference in olfactory improvement between patients who underwent middle turbinate resection and those who did not. Olfactory dysfunction includes conductive, neural, and mixed types [4]. Many scholars believe that CRSwNP-induced olfactory dysfunction is caused by two different mechanisms: First, nasal mucosal swelling, polyp formation, and secretion blockage in the olfactory cleft obstruct air flow to the olfactory cleft, affecting the binding of odor molecules to olfactory neurons, leading to conductive olfactory dysfunction [32,33]. Second, inflammatory factors such as TNF-α-mediated inflammation infiltrate the olfactory epithelium, causing damage to olfactory receptor neurons and leading to neural olfactory dysfunction [33-35]. In the nECRSwNP group, the main factor causing olfactory dysfunction may be conductive olfactory dysfunction due to obstruction, where the middle turbinate plays a crucial role in air flow into the olfactory cleft [6,33,34]. As a result, patients in the nECRSwNP group who underwent middle turbinate resection had enhanced nasal ventilation, leading to an improvement in olfactory function. In the ECRSwNP group, although FESS surgery also resolved the conductive factors causing olfactory dysfunction, the ECRSwNP group is characterized by type II inflammation, which includes increased eosinophils, IL-5, IL-13, and IgE levels. The increase of these inflammatory factors causes damage to olfactory neurons, leading to a predominance of neural olfactory dysfunction [28,29]. Intraoperative middle turbinate resection only solves the obstructive factors but cannot solve the damage caused by inflammatory factors to olfactory neurons. Hence, middle turbinate resection during surgery does not significantly impact olfactory recovery in the ECRSwNP group.

In summary, the middle turbinate plays an important role in directing airflow in the nasal cavity and protecting the olfactory region. We believe its effect on improving olfaction is mainly reflected in two aspects: First, it improves nasal airflow, allowing odor molecules to more easily reach the olfactory cleft. Second, appropriate middle turbinate resection helps alleviate the inflammatory burden, reducing mucosal swelling and obstruction caused by chronic inflammation, thereby further promoting olfactory recovery. Although middle turbinate resection has the potential to improve olfaction, its long-term effects and potential drawbacks should not be overlooked. First, middle turbinate resection may lead to instability in the nasal structure, altering the dynamics of nasal airflow, which in turn can affect the overall function of the nasal cavity. Second, excessive resection may result in nasal dryness and local mucosal damage, increasing the risk of infection, and potentially impacting the recovery of other nasal functions. Regarding the long-term effects of middle turbinate resection, although the follow-up period in this study was only 6 months, previous studies have suggested that the benefits of middle turbinate resection may continue to manifest with long-term follow-up [36,37]. Specifically, resection of the middle turbinate may help reduce the recurrence of chronic sinusitis in patients and maintain long-term olfactory improvement by improving airflow and reducing the inflammatory burden. However, some studies have pointed out that excessive resection of the middle turbinate may lead to long-term nasal dryness and other structural issues [9,10], so in actual surgery, how to balance the strategy of resecting versus preserving the middle turbinate remains an issue that deserves attention.

To thoroughly evaluate the impact of different middle turbinate management approaches on postoperative olfactory recovery, we conducted comparisons using two distinct classification methods. The first method categorized middle turbinate resection into four types: A-MT, C-MT, L-MT, and P-MT. The second method grouped them into partial middle turbinate resection (A-MT, L-MT, and P-MT) and complete middle turbinate resection (C-MT). Our findings revealed that, although there were differences in preoperative subjective VAS scores and olfactory TDI scores between the complete resection (C-MT) group and the partial resection group—with the C-MT group exhibiting higher VAS scores and lower olfactory TDI scores—no significant differences in olfactory improvement were observed among the groups at 6 months postoperatively, regardless of the classification method applied.This may be because the choice of middle turbinate surgical approach was entirely based on the surgeon's imaging examination and clinical experience, rather than random assignment. This is the same as the findings of Saedi [38] and Bolger [6], who reported that for most patients, "partial" or "limited" turbinateoplasty, although different in surgical approach, has little impact on olfaction. Delarestaghi [30] suggested that otolaryngologists should advocate limited middle turbinate resection techniques, restricting the resection to the lower bulbous part of the middle turbinate while preserving the high lamellar part. Akiyama [39] proposed and advocated for submucosal resection of the lower bulbous part of the middle turbinate, removing only the bone while preserving the submucosa and mucosal tissue to maintain olfactory function. Based on the findings of this study, although complete middle turbinate resection (C-MT) and partial middle turbinate resection show no significant difference in their impact on postoperative olfactory recovery, we recommend that the extent of middle turbinate resection be carefully considered for patients with chronic rhinosinusitis with nasal polyps (CRSwNP), particularly those with significant anatomical abnormalities of the middle turbinate. This recommendation is based on the following considerations: 1) the root of the middle turbinate serves as a critical anatomical landmark in revision surgery, and 2) the medial mucosa of the middle turbinate contains a population of olfactory neurons. Therefore, the resection strategy should be tailored to individual patient conditions to promote olfactory recovery, while unnecessary excessive resection, especially complete middle turbinate resection, should be avoided whenever possible. For ECRSwNP patients primarily characterized by Type II inflammation, in addition to addressing the pathological changes of the middle turbinate during surgery, postoperative comprehensive treatment focused on controlling Type II inflammation remains crucial for the recovery of olfactory function.

Limitations

This study has several limitations that should be considered when interpreting the findings. First, the sample size (n=72) may limit the generalizability of the results, particularly when subgroup analyses are performed. Although the sample size was sufficient to provide initial insights into the effects of middle turbinate resection on olfactory function, larger sample sizes in future studies would help validate and extend the findings. Second, the follow-up duration of 6 months may not be sufficient to fully assess long-term olfactory recovery, as olfactory function could continue to improve or fluctuate over a longer period. Future research with extended follow-up periods will be necessary to gain a more comprehensive understanding of the stability and duration of recovery. Third, although our study did not find a statistically significant difference in the impact of different middle turbinate resection approaches on postoperative olfactory recovery, the choice of surgical technique was based on the surgeon's clinical judgment and imaging findings, rather than random assignment. This potential selection bias, coupled with the limited sample size, may affect the ability to draw definitive conclusions about the influence of different resection techniques on olfactory function. Lastly, as all patients were operated on by the same senior rhinologist, this single-surgeon approach, while minimizing technical variability, may limit the generalizability of the results to other surgical settings. Future studies involving multiple surgeons and centers would provide broader applicability of the findings.

Conclusion

This study explored the impact of middle turbinate resection on postoperative olfactory recovery in patients with CRSwNP of different pathological subtypes. We found that the severity of nasal polyps and whether middle turbinate resection was performed during surgery significantly affected postoperative olfactory recovery in CRSwNP patients. Middle turbinate resection demonstrated sustained olfactory improvement in patients with different pathological subtypes of CRSwNP, while the improvement in the middle turbinate preservation group plateaued around three months post-surgery. In the nECRSwNP group, the proportion of patients with significant olfactory improvement was higher in those who underwent middle turbinate resection compared to those who had middle turbinate preservation. However, in the ECRSwNP group, there was no significant difference in olfactory improvement between patients who underwent middle turbinate resection and those who did not. Although different methods of middle turbinate resection did not significantly affect the degree of olfactory recovery, overall, middle turbinate resection played an important role in promoting olfactory recovery. Future research should focus on optimizing the methods of middle turbinate resection and exploring more personalized treatment strategies to achieve better postoperative olfactory recovery outcomes.

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Authorship contribution

FTJ: data curation, methodology and writing; JHL: data curation, writing; RRG: investigation, data curation; QTY: supervision, visualization, writing and original draft preparation; SW: supervision, visualization, writing and original draft preparation.

Conflict of interest

The authors report no conflicts of interest in this work.

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