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Central Compartment Atopic Disease and Its Surgical Outcomes: Olfactory Changes and Technical Notes

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Abstract

Background: Central compartment atopic disease (CCAD) is a recent, novel phenotype of chronic rhinosinusitis. Only a few studies have assessed olfactory function in patients with CCAD.

Objectives: We aimed to investigate olfactory function changes after functional endoscopic sinus surgery (FESS) in patients with CCAD and proposed some surgical techniques to enhance the postoperative olfactory outcomes in such patients.

Design: A retrospective cohort study.

Methods: We collected data from 23 patients (8 men and 15 women) with CCAD who underwent FESS performed by a surgeon in Taiwan, between June 2018 and December 2021. The demographic data, olfactory function, and serum and tissue eosinophil percentages of the included patients were analyzed. The Top International Biotech Smell Identification Test (TIBSIT; Top International Biotech, Taipei, Taiwan) was used to assess olfactory function.

Results: Of the 23 patients, most (95%) showed a positive reaction to aeroallergens, and 2 patients (8.7%) had asthma. Ten patients (43.5%) had peripheral eosinophilia, and 9 (39%) had eosinophilic nasal polyps. Moreover, the patients presented with variable olfactory dysfunction; the mean preoperative TIBSIT (pr-TIBSIT) score was 12.8 ± 2.3 (range: 0-43), whereas the mean postoperative TIBSIT (po-TIBSIT) score was 29.2 ± 1.9 (range: 16-44). The po-TIBSIT score was significantly better than the pre-TIBSIT score (paired *t* test, $P < .0001$). The improvement in olfactory function was not significantly correlated with the patients' age, serum eosinophil percentages, and nasal polyp eosinophil counts.

Conclusion: Our findings indicate that CCAD is significantly associated with olfactory dysfunction and that FESS can effectively improve olfactory function. To optimize postoperative olfactory outcomes, precise removal of polyps from the olfactory cleft without damaging the neuroepithelium is recommended. Our study provides valuable insights into the management of CCAD patients undergoing FESS and can guide surgical decision-making to achieve optimal olfactory function outcomes.

Keywords: central compartment atopic syndrome, chronic rhinosinusitis, functional endoscopic sinus surgery

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Introduction

Chronic rhinosinusitis (CRS) is classically categorized into 2 major phenotypes: CRS without nasal polyps and CRS with nasal polyps (CRSwNP). Central compartment atopic disease (CCAD) is a recent and novel phenotype of CRS.[1–8] The elaboration of CRS endotypes is promising in terms of determining treatment approaches for CRS.[9] However, CCAD is a unique CRS variant and needs to be identified in patients with CRS.

Central compartment atopic disease represents a distinct inhalant allergy-related inflammatory process that occurs in the central compartment of the nasal and sinus cavity. The middle turbinate

(MT), superior turbinate (ST), and posterosuperior nasal septum (PSNS) are the major vulnerable sites for CCAD.[3] Because the central nasal cavity is one of the main affected sites, impaired olfactory function is quite common in patients with CCAD.[10–12]

Herein, we aimed to investigate the long-term olfactory function changes after functional endoscopic sinus surgery (FESS) in patients with CCAD; we also assessed the indicators for smell recovery and proposed some surgical techniques for improving surgical outcomes.

Patients and Methods

Central Compartment Atopic Disease Criteria

Any patient who complained of nasal speech or anosmia drew our attention. Such patients were subjected to computed tomography (CT) scanning and nasoendoscopy for CCAD diagnosis (Figures 1 and 2).

We have been diagnosing patients with CCAD at our clinic since 2017. The edematous mucosa, polypoid mucosa, and true polyps, which occur in the medial aspect of MT, the ST, and the PSNS, respectively, are the major central compartment lesions. Once the major lesion was confirmed, an extension of the major lesion to the lateral aspect of MT, or even to the osteomeatal complex or ethmoid cells, was considered acceptable. Mild maxillary and frontal recess involvement were acceptable. Frontal recess lesions are an extension of central compartment lesions.[3]

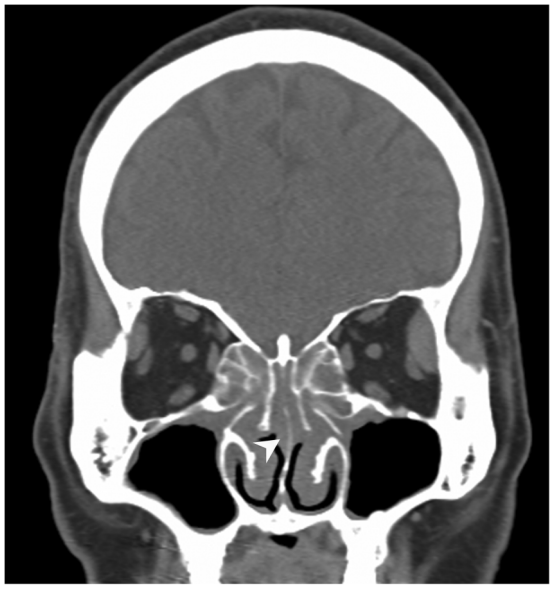

Figure 1. Typical central compartment atopic disease (CCAD): severe central compartment soft tissue thickening (white arrow head) with bil. osteomeatal complex obstructed.

Data Collection

We retrospectively collected data from patients fulfilled with abovementioned CCAD criteria who underwent FESS performed by a surgeon (PHS) at the Kuang-Tien General Hospital, Taiwan, between June 2018 and December 2021. This study was approved by the institutional review board of our hospital (KTGH #11151).

Inclusion criteria: According to endoscopic examination and sinus CT scanning findings of inflammation/polypoid changes located within the central compartment (PSNS, MT, ST).

Exclusion criteria: Patients who received sinus surgery previously, unilateral or isolated sinusitis. Patients fulfill other subtypes of CRS, such as allergic fungal rhinosinusitis. Patients who had an autoimmune disease, long-term systemic corticosteroid usage, and under psychiatric treatment.

Physical Examinations and Laboratory Testing

Olfactory Function Tests

The Top International Biotech Smell Identification Test (TIBSIT; Top International Biotech) was used to evaluate the patients' preoperative and postoperative olfactory functions.[13]

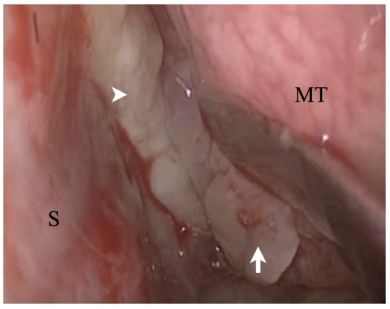

Figure 2. Nasoendoscopy image of typical central compartment atopic disease (CCAD): mucosal polypoid change of posterosuperior nasal septum (white arrow head) and polyps in medial aspect of middle turbinate. (white arrow) MT, middle turbinate; S, septum.

As a "Traditional Taiwan-version" of UPSIT, the TIBSIT using more familiar odors for Taiwanese people. It consists of 16 tests with an odorant embedded in fragrant microcapsules positioned on a strip. Each test scores from 0 to 3, hence, the maximum score is 48 points (perfect olfactory function) for the 16 tests. The TIBSIT has been readily adopted domestically.[14]

We performed 1 test preoperatively and at least 2 tests postoperatively. The preoperative TIBSIT (pr-TIBSIT) was mostly acquired a few days before the operation, whereas the first postoperative TIBSIT (po-TIBSIT) was mostly acquired 3 to 4 weeks after the operation. The patients were asked to revisit the hospital for a smell test at least once every year. The last-visit TIBSIT (lv-TIBSIT) results were recorded for comparison. Improvement exceeding 5 points (10% of the total score 48) was considered significant.[15] Less than 5-point changes in the TIBSIT score between 2 testing episodes indicated "no change."

Allergen Tests

Aeroallergen sensitization was evaluated through serologic assessments based on an automated microfluidic-based immunoassay system (BioIC), which is comparable to the ImmunoCAP assay.[16] The cutoff value for allergen sensitization in this test was 1.0 AU.[17]

Eosinophil Count

Peripheral eosinophil counts are presented as the percentage of total leukocytes. Tissue eosinophil counts were calculated by pathologists and are presented as the number of tissue eosinophils per high-power field (n/HPF). An absolute count of >55 eosinophils per HP was considered to indicate high tissue eosinophilia.[18,19] The cutoff value for high peripheral blood eosinophils was set at 5%.[5,20]

Asthma

Asthma was diagnosed based on the Global Initiative for Asthma guideline.[21]

Medical Treatment and Surgical Techniques

Medical Treatment

Before FESS, all the patients received appropriate medical treatment with intranasal saline irrigation and intranasal corticosteroids usage at least one month. Postoperative management included a 6-week course of 1.0 g of clarithromycin antibiotic daily, intranasal saline irrigation, and topical steroids at night after nasal irrigation. Oral steroids were not given unless the patient was noted to have massive polypoid changes during postoperative endoscopy.

Surgical Techniques

Standard FESS was performed according to the disease-involved area, including submucous resection of the inferior turbinate, septoplasty, unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, and frontal sinus procedures.

The central compartment lesions were directly visualized using a zero-degree endoscope. Septal deviations, if any, were corrected before approaching the central compartment. A microdebrider was used to approach the polypoid tissue over the medial aspect of the MT. The microdebrider was gently slid in and firmly attached to the mucosal surface of the MT. A little force was applied to the MT laterally to ensure that the "blade" side was toward the polyp and not the mucosal surface of the MT. The polyp, which had been sucked into the tunnel of the blade, was then debrided (Figure 2). The debrider's "non-blade" side was maintained at the mucosal surface of MT from the bottom to the top. Leaving the handpiece away from the mucosal surface of the MT increases the chance of damaging it. We ensured avoidance of a "blade" side-flip in another direction during the whole procedure.

After the surgery was completed, we used a "sandwich" approach for nasal packing. Bioresorbable nasal dressing was used for both the medial and lateral aspects of the MT to maintain the MT in the "middle" position of the sinus cavity (Figure 3). We used this technique because we wanted to establish more patent airflow spaces in the olfactory cleft (OC), as well as avoid adhesion or synechia of the MT to the septum.

Statistical Analysis

All of the data are presented as the mean ± standard error of the mean. A paired t test was used to compare the TIBSIT recorded at different time points but in the same patient group. Pearson's chi-square test and Fisher exact test were used to analyze dichotomous data. The ordinal scales

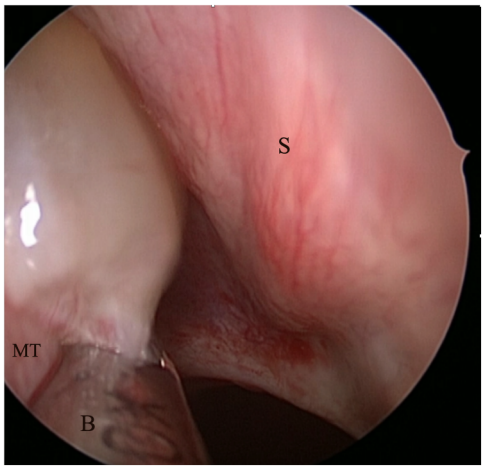

Figure 3. The microdebrider blade sucked the polyp in then gently debride it, and carefully preserved the mucosa of middle turbinate and septum. MT, middle turbinate; B, blade side of microdebrider; S, septum.

relationship was assessed using the Spearman rank-order correlation test. All tests were 2-tailed. A P value <.05 was considered statistically significant.

Results

A total of 23 patients with CCAD [8 men (mean age: 53.9 ± 2.8, range: 41-62 years) and 15 women (mean age: 51.5 ± 4.1 years, range: 21-74 years)] were enrolled in this study. The mean follow-up duration was 28.5 ± 2.6 months (range: 8-50 months). Aeroallergen-positivity was noted in 19 of 20 patients (the remaining 3 patients did not undergo allergen tests). The mean Lund-Mackay CT score[22] was 10.8 ± 4.6, range: 4 to 18. Asthma was found in only 2 patients (8.7%). The mean serum eosinophil percentage was 4.8% ± 0.7% (range: 0.7%-13.2%). In 10 patients, this value was >5%, indicating peripheral eosinophilia. The mean nasal polyp eosinophil count was 50.6 ± 10.7/HPF (range: 0-200/HPF; 9 patients had a value of >55/HPF and were classified as having eosinophilic nasal polyps). The mean pr-TIBSIT was 12.8 ± 2.3 (range: 0-43), and the mean po-TIBSIT score was 29.2 ± 1.9 (range: 16-44); the patients' demographic data are shown in Table 1. In 2 patients (cases 10 and 11), the TIBSIT score after surgery did not improve by 5 points; however, case 11 continued to report improved olfactory function over time. The mean lv-TIBSIT was 31.5 ± 2.3 (range: 16-48). The po-TIBSIT score was significantly better than the pr-TIBSIT score (paired t test, P < .0001; Figure 4), whereas the lv-TIBSIT score was not significantly different from the po-TIBSIT score (P = .10; Figure 4).

The difference between the po-TIBSIT and pr-TIBSIT scores was considered the "immediate recovering TIBSIT (ir-TIBSIT)" score; moreover, the difference between the lv-TIBSIT and po-TIBSIT scores was defined as the "long-term maintaining TIBSIT (ltm-TIBSIT)" score (Figure 5). "Significant improvement" was defined as a score improvement of >4 points. The mean ir-TIBSIT score was 16.4 ± 2.0 (range: 1-37), whereas the mean ltm-TIBSIT score was 2.3 ± 1.4 (range: −11 to 20).

The ltm-TIBSIT and ir-TIBSIT scores were not significantly correlated with the patients' age, serum eosinophil percentages, and nasal polyp eosinophil counts (Spearman's rank correlation, P > .05). When smell changes were categorized into significant (+) and non-significant (–) and eosinophilia was categorized into high and low, a 2-by-2 cross table was obtained (Table 2), and the results showed that smell changes of neither ir-TIBSIT nor ltm-TIBSIT were significantly correlated with peripheral eosinophilia or eosinophilic nasal polyps; however, we found no significance for the association of ltm-TIBSIT and tissue eosinophilia (P = .062), indicating that patients with a high tissue eosinophil percentage tend to show improved olfactory function after surgery and proper medicine control over time.

Discussion

Central compartment atopic disease is a new phenotype of CRS and is closely related to aeroallergen sensitization. It mainly occurs in the central part of the nasal cavity, such as the MT, ST, and PSNS. Although patients with CCAD are mostly aeroallergen-positive, some studies have shown that the aeroallergen prevalence is lesser among such patients,[10,11] perhaps owing to local allergic response without systemic manifestation and lower sensitivity to serum allergen tests (ImmunoCAP) than to the traditional skin-prick test. However, in our study, we found aeroallergen-positivity in 19 of the 20 (95%) patients. The only difference was that we used BioIC for our serum tests. The accuracy of aeroallergen testing using ImmunoCAP and BioIC among patients with CCAD needs to be further investigated.

Table 1. The Patients' Demographic Data.

No.	Gender	Age	Asthma	Allergen	LMS	Surgery	pr-TIBSIT	po-TIBSIT	lv-TIBSIT	p-eos	t-eos	fo-month
1	Female	74	0	1	18	FESS	8	17	20	0.70%	0	27
2	Female	53	0	1	17	FESS	4	27	21	1.00%	0	46
3	Female	60	0	1	18	EMLP	6	25	22	2.20%	200	50
4	Male	54	0	1	17	FESS, SMP	6	18	16	2.20%	10	25
5	Female	62	0	1	13	FESS, SMP	14	33	28	1.60%	150	40
6	Female	67	0	x	17	FESS, SMP	4	21	23	0.80%	80	27
7	Male	61	0	1	7	FESS, SMR	2	18	19	3.00%	10	10
8	Male	41	0	1	11	FESS, SMP	26	43	43	4.50%	0	14
9	Female	38	0	0	5	FESS, SMP	16	32	35	2.70%	30	8
10	Male	48	0	1	9	FESS, SMR	34	38	37	3.60%	10	21
11	Female	43	0	1	5	FESS	18	21	29	5.60%	75	21
12	Female	39	0	1	8	FESS	6	42	44	8.00%	70	12
13	Male	59	0	1	11	FESS, SMP	12	22	24	3.70%	40	25
14	Female	56	1	1	12	FESS	14	28	30	13.00%	100	11
15	Female	68	0	x	5	FESS, SMP	15	31	20	5.10%	8	34
16	Male	62	0	1	9	FESS, SMP	16	22	23	5.90%	20	36
17	Female	52	0	1	5	FESS, SMP	7	26	46	9.00%	40	38
18	Female	59	0	1	14	FESS	7	44	48	6.20%	30	40
19	Male	62	0	1	8	FESS, SMP	3	29	41	2.70%	80	44
20	Female	59	0	x	10	FESS, SMP	2	33	45	2.50%	80	48
21	Female	21	0	1	15	FESS, SMP	31	42	44	5.00%	0	27
22	Female	21	1	1	10	FESS, SMT	3	16	22	13.20%	80	27

(Continued)

Table 1. Continued.

No.	Gender	Age	Asthma	Allergen	LMS	Surgery	pr-TIBSIT	po-TIBSIT	lv-TIBSIT	p-eos	t-eos	fo-month
23	Male	44	0	1	4	FESS, SMP	43	44	44	7.60%	50	25

Abbreviations: LMS, Lund-Mackay score; FESS, functional endoscopic sinus surgery; EMLP, endoscopic modified Lothrop procedure; SMP, septomeatoplasty; SMR, submucosal resection of septum; SMT, submucosal turbinectomy; pr-TIBSIT, preoperative TIBSIT; po-TIBSIT, postoperative TIBSIT; lv-TIBSIT, last-visit TIBSIT; p-eos, peripheral eosinophil; t-eos, tissue eosinophil; fo-month, follow-up months.

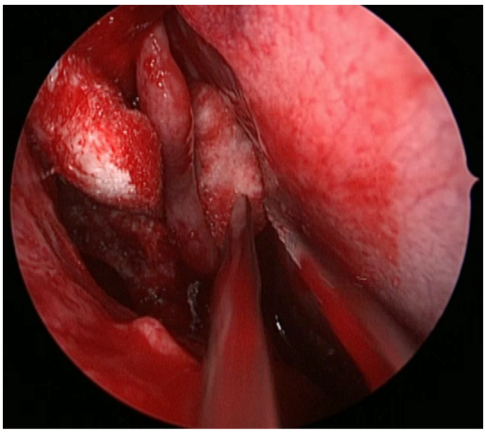

Figure 4. "Sanwich"packing fashion: "Sandwich" packing fashion for central compartment atopic disease (CCAD) patients on the right sinus cavity. The middle turbinate was maintained in the central position between middle turbinate and septum. The forceps shown in this figure are in between the septum and middle turbinate.

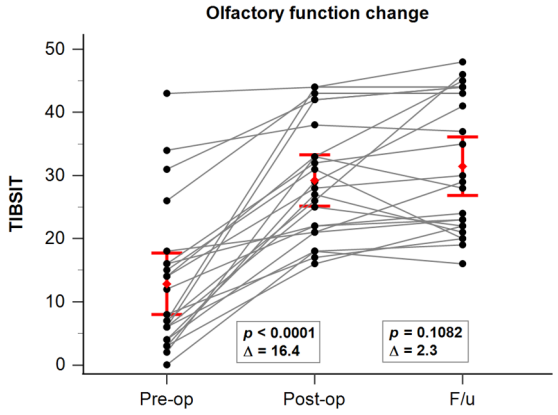

Figure 5. The preop Top International Biotech Smell Identification Test (TIBSIT) score was significantly better than the postop TIBSIT score (paired *t* test, $P < .0001$), whereas the lv-TIBSIT score (follow up, f/u) was not significantly different from the post-op TIBSIT score ($P = .10$).

The prevalence of asthma is approximately 6% to 17% among patients with CCAD.[5,6,8,10,11] Although the prevalence of asthma among the patients with CCAD was not very high as compared to that among patients with CRSwNP, race-related differences should be studied in detail. In a study conducted in southeastern United States, involving mainly Caucasian, African American patients, the prevalence of asthma was 17.1% among those with CCAD but 37.1% among those with CRSwNP.[8] In a study involving Asian patients, the prevalence of asthma was 9.8% among those with CCAD patients, which was significantly higher than the 3.5% prevalence noted among those with CRSwNP.[11] In the present study, only 2 (8.7%) patients were found to have asthma. Despite the low prevalence of asthma among Asian patients with polyps,[23] asthma, as a comorbidity, is still worth noticing among Asian patients with CCAD.

Another interesting issue is preoperative olfactory function among patients with CCAD. Some studies have shown better or intact olfactory function among those with CCAD than among those with other types of CRS.[1,6] Moreover, some studies conducted in Asia have demonstrated that hyposmia or anosmia is the major symptom of CCAD[10,11] In Chinese patients, it seemed that CCAD represents a type II inflammation endotype and had greatly affected in olfactory function.[10]

These contradictory results may be attributable to the different stages of CCAD and different races. During early CCAD, only edema and/or polypoid changes are encountered, and further progression of the polyps is possible in the late stage.[3] Olfactory function may remain intact at early

Table 2. The Correlation Between Recovering Domain and Eosinophil Levels.

		ir-TIBSIT			ltm-TIBSIT		
		Sig.(+)	Sig.(–)	*P* value	Sig.(+)	Sig.(–)	*P* value
Blood eosinophil	High	8	1	.78	3	6	.49
	Low	12	1		2	11	
Tissue eosinophil	High	8	1	.78	4	5	.062
	Low	12	1		1	12	

Abbreviations: ir-TIBSIT, immediate-recovering Top International Biotech Smell Identification Test; ltm-TIBSIT, long-term maintaining Top International Biotech Smell Identification Test; eos, eosinophil; Significant improvement definition: TIBSIT improved >4 points.

stages but become impaired at a later stage. Unless olfactory dysfunction becomes apparent, early-stage CCAD might not be easy to identify. In our study, only one patient (case 23) had normal smell identification test results before surgery. In the current clinical settings, if a patient complains of smell loss or just nasal speech without nasal blockage, we routinely check the central compartment thoroughly.

Peripheral and tissue eosinophilia were not uncommon among our patients. Eosinophilia was found in 10 (43.4%) peripheral blood samples and 9 (39.1%) tissue samples, which is comparable to the percentage of peripheral eosinophilia (35.5%) reported by a previous study.[5] Moreover, Lin et al found that the peripheral eosinophil counts were significantly higher among those with CCAD than among other types of CRS.[10] In the present study, we found that neither peripheral eosinophilia nor tissue eosinophilia was significantly related to smell changes (ir-TIBSIT and ltm-TIBSIT), implying that smell recovery depends on the eradication of OC polyps and the subsequent maintenance of the patency of the OC rather than the eosinophilic burden. Interestingly, Preeti et al also found that OC opacification correlated with objective measures of olfaction among patients with CRS.[12] In our patient cohort, we observed that the extent of polyposis over OC (including the posterosuperior septum and medial side of the MT) correlated well with the objective smell test results. In other words, a patient's claim that they experienced a deterioration in their smelling ability recently after surgery was always considered a sign of progressive polypoid or edematous changes over the central compartment. Cases 2, 5, and 15 were found to have experienced significant olfactory deterioration between their last-visit smell test and postoperative smell test; endoscopic examination showed that patients 2 and 5 had edematous changes over the central compartment, whereas patient 15 had significant polyp regrowth over the OC. The remaining 20 patients were found to have a clean central compartment, as revealed by endoscopy performed during the follow-up periods. A previous study also reported the phenomenon of low polyp recurrence rates among patients with CCAD.[7]

In the present study, a substantial improvement in olfactory function was noted for almost every patient, indicating that the smell loss faced by patients with CCAD can be reversed by carefully removing the polyps or polypoid lesions in the OC. Kuperan et al found that OC polyp surgery can improve olfactory function outcomes by the 6-month postoperative follow-up[24]; they used a 60-degree curved microdebrider blade to remove the olfactory polyps but did not describe the surgical technique in detail. In our opinion, the optimal surgical technique for patients with CCAD is as follows. The main principle of our surgical technique involves allowing the polyps to be suctioned into the microdebrider tunnel rather than aggressively confronting the polyps and debriding them. Aggressive polyp debridement is associated with a higher risk of injury to the mucosa and olfactory neuroepithelium. Moreover, iatrogenic endoscopic sensory olfactory injuries could frequently occur with epithelial resection in the nasal vault, either medially during septoplasty or submucous resection of the septum or laterally

in between heroic attempts to "clean out every ethmoidal cell."[25] Particularly in patients with CCAD, OC lesions deserve sophisticated endoscopic management rather than ignorance. Septoplasty with or without turbinate surgery (Table 1) seems to improve olfactory function,[26] so we routinely perform septoplasty or/and turbinoplasty if any deviated septum or/and hypertrophied turbinates were encountered. Olfactory function improvement can be achieved postoperatively once the majority of polypoid lesions are removed and the olfactory neuroepithelium is well-preserved. Moreover, long-term maintenance of olfactory function may be achieved either by avoiding inhalant allergens or through appropriate medical treatment.

Limitation

Several limitations of the current study should be discussed. Firstly, the absence of a control group and the limited number of cases raise questions about the reliability of the olfactory outcomes achieved through our surgical techniques and packing method. As this study was conducted retrospectively, it was challenging to find a comparable group that underwent "subtotal" polyp removal (as opposed to our near-total removal) or received only "packing over the osteomeatal complex" (as opposed to our sandwich packing). However, we believe that meticulous management of the OC can lead to favorable olfactory results.

Secondly, we did not collect data using a quality-of-life questionnaire for these patients. While there are numerous articles addressing various aspects of surgical outcomes, our focus was primarily on the recovery of olfactory function after precise surgical techniques in CCAD patients. Initially, we did not collect subjective symptom data using tools like the Visual Analog Scale or the Sinonasal Outcome Test-22, relying solely on objective smell tests. Nonetheless, we plan to conduct further studies specifically related to the quality of life of CCAD patients in the future.

Thirdly, we did not compare the olfactory outcomes with other phenotypes of CRS. The etiological heterogeneity of CRSwNPs and the wide range of disease severity pose challenges in establishing meaningful comparisons.

Conclusion

We found that CCAD is strongly associated with olfactory dysfunction and that FESS leads to significant improvements in olfactory function improvement. Long-term olfactory function was maintained in most patients in this study. However, the olfactory function improvement was not associated with the patients' age and serum and nasal polyp eosinophil percentages. Precisely removing the polyps from the OC without damaging the neuroepithelium is crucial for improving olfactory function. A special "sandwich" approach using bioresorbable nasal dressing for postoperative nasal packing of the medial and lateral aspects of the MT might help avoid MT adhesion and synechia, thereby ensuring better olfactory outcomes. Our results provide valuable insights for clinicians treating patients with CCAD and how to maintain long-term olfactory function.

Declarations

Authors' Note

Sheng-Kai Huang and Ching-Hung Hsieh contributed equally to this article. *Ethics Approval:* The local medical ethical committee (Institutional Review Board of Kuang Tien General Hospital) approved this study (KTGH 11151), and consent to participate was waived. *Availability of Data and Materials:* Available on request.

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Declaration of Conflicting Interests

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