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Association between cognition and olfaction-specific parameters in patients with chronic rhinosinusitis

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Abstract

Background Patients with chronic rhinosinusitis (CRS) have reported significantly cognitive and olfactory dysfunction. This study aimed to explore the relationship between cognitive function and olfaction-specific parameters in patients with CRS.

Methods A cross-sectional survey method was used to investigate 98 participants, including 75 patients with CRS and 23 healthy controls. Cognitive function and psychophysical olfactory tests were performed. Olfactory cleft endoscopy scale and olfactory cleft computed tomography (CT) scores were obtained. Multivariate logistic regression was used to analyze the risk factors of Mild Cognitive Impairment (MCI) in patients with CRS.

Results There are significant differences in age, Montreal Cognitive Assessment (MoCA) scores, number of MCI, Lund-Mackay olfactory cleft (LM-OC) score, and blood eosinophil count between CRS with and without olfactory dysfunction groups (all $P<0.05$). Total MoCA scores were positively correlated with thresholds-discrimination-identification (TDI) score ($r=0.541$, $P<0.001$), olfactory threshold (OT) ($r=0.440$, $P<0.001$), olfactory discrimination (OD) ($r=0.541$, $P<0.001$), and olfactory identification (OI) ($r=0.382$, $P=0.001$) scores. Furthermore, total MoCA scores were negatively correlated with LM-OC scores ($r=-0.351$, $P=0.002$). After adjusting for patient demographics, only the OD score was an independent risk factor for MCI among patients with CRS (odds ratio = 0.792; $P=0.039$). The OD scores less than 11.5 were the best predictor of MCI in patients with CRS.

Conclusion Olfaction-specific clinical parameters were highly correlated with cognitive function in patients with CRS and the OD score was an independent risk factor for MCI in patients with CRS.

Keywords Chronic rhinosinusitis · Olfactory dysfunction · Cognitive dysfunction · Anosmia · MoCA · Predictor

Introduction

Chronic rhinosinusitis (CRS) is a common chronic sinonasal disease with a prevalence ranging from 10 to 12% [1]. Olfactory dysfunction is one of the main symptoms of patients with CRS, affecting up to 80% of patients with CRS [2]. CRS-associated olfactory dysfunction is caused by mucosal inflammation, which leads to olfactory epithelial damage or physical obstruction of the olfactory cleft. The nasal blockage leads to the inability to transmit odors to the olfactory cleft area. The inflammatory reaction in the vicinity of the olfactory cleft reduces the transmission of olfactory nerves, which eventually leads to a decrease in the volume of the olfactory bulb [3]. Moreover, sinonasal inflammation can cross the blood–brain barrier into the brain via the olfactory bulb and olfactory nerves, which affects olfactory transmission pathways and brain organization [4].

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Symptomatology and manifestations of CRS has a huge impact on the quality of life (QOL) of patients, ranging from rhinology symptoms of nasal obstruction, nasal discharge, and headache to cognitive decline, including central behavioral fatigue, depression, reduced sleep, reduced attention, slowed thinking, and memory impairment [5–7]. The association between CRS and cognition has been demonstrated in previous studies. Patients with CRS were more likely to progress to dementia [8], and the prevalence of CRS was higher in patients with dementia than healthy controls [9]. Moreover, patients with CRS had worse cognitive function than control subjects without a history of sinusitis [5]. After medication or surgery on patients with CRS, significant improvements in cognitive function were found [10–12]. Olfactory dysfunction is positively related to increased medication use and decreased QOL [13, 14], which may increase the risk of major depression [15] and the economic burden of patients [16, 17]. Previous studies have shown a strong relationship between olfactory decline and cognitive impairment, and olfactory function can be used as a screening indicator for high-risk cognitive impairment before the development of mild cognitive impairment (MCI) or dementia [18, 19]. However, it is unclear whether the relationship of olfaction and cognition exists in patients with CRS and whether olfaction can predict the occurrence of MCI in patients with CRS have not been explored.

Based on the above findings, we assumed that olfactory decline may be associated with cognitive function and that examination of olfactory-specific parameters may help to screen for the risk of cognitive dysfunction in patients with CRS. In this study, we explore the association between olfactory function and cognitive function in patients with CRS and then examine the predictive significance of olfaction-specific parameters for cognitive dysfunction in patients with CRS.

Materials and methods

Patients with a diagnosis of CRS based on the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS20) and controls with the non-inflammatory disease from December 2021 to October 2022. All participants underwent a series of specialized otorhinolaryngological and cognitive examinations, which included sinus computed tomography (CT), nasal endoscopy, olfactory psychophysical test (Sniffin' Stick test), outcome measure for CRS (the 22-item Sino-Nasal Outcome Test, SNOT-22) and neuropsychological testing (Montreal Cognitive Assessment, MoCA). Demographic characteristics were further collected. Exclusion criteria included: (1) any cancer, tumor, or chronic disease which has the potential to affect cognition and olfaction (2) uneducated or non-Mandarin Chinese speakers (3) autoimmune disease, ciliary dysfunction, cystic fibrosis, autoimmune disease, immunodeficiency (4) craniocerebral surgery, stroke, or brain trauma (5) antibiotics or any topical/systemic steroids medication in the last 4 weeks (6) patients who does not complete the whole test. Before treatment, 15 ml of peripheral venous blood was gathered from each subject in an EDTA anticoagulation tube. A complete peripheral blood cell count was performed by an automated analyzer (Beckman Coulter, Miami, Florida), and the blood eosinophil and basophil counts were calculated. All patients signed informed consent before participation. The flow diagram of the study design was shown in Fig. 1.

Cognitive function assessment

Cognitive function was assessed by Montreal Cognitive Assessment 7.0 (MoCA 7.0). MoCA was invented by Prof. Nasreddine according to clinical experience and MMSE scoring criteria in 2004 [20]. It was widely used as an assessment tool for the rapid screening of MCI. The 30-point total MoCA score covers seven cognitive domains: visuospatial/executive (trail-making test: 1 point, copy tube: 1 point, clock drawing task: 3 points), attention (forward digit span: 1 point, backward digit span: 1 point, vigilance: 1 point and serial subtraction: 3 points), naming (3 points), delayed recall (5 points), language (verbal fluency: 1 point, sentence repetition: 2 points), abstraction (2 points), and orientation (6 points). It indicated as MCI if the total scores were < 26. Furthermore, the total scores will be added one point if the education year is less than 12 years [21]. The basic principle of the test is to be done in a quiet environment, with subjects with no inhibitions and staying awake. It takes approximately 10 min to complete the test. MoCA has been proven to be appropriate in the Chinese population in previous studies [22–25].

Olfactory function assessment

Olfaction function was examined by the Sniffin' Sticks (Burghart Instruments, Germany). The assessment of olfactory function includes olfactory threshold (OT), olfactory discrimination (OD), olfactory identification (OI), and the sum composite scores (threshold, discrimination, and identification, TDI) [26]. Subjects were not allowed to smoke, eat, or drink anything but water for fifteen minutes before the test. The OT test used different concentrations of n-butanol, using a single-step, triple-forced selection, subjects selected the correct triplet pen and then replaced it with a lower concentration. The OD test used a triplet of pens, containing two of the same odors and one of a different odor, selecting different odors and counting one point. Sixteen odor pens were used in the OI test, and participants selected the odor that matched the options given. Each odor must be smelt

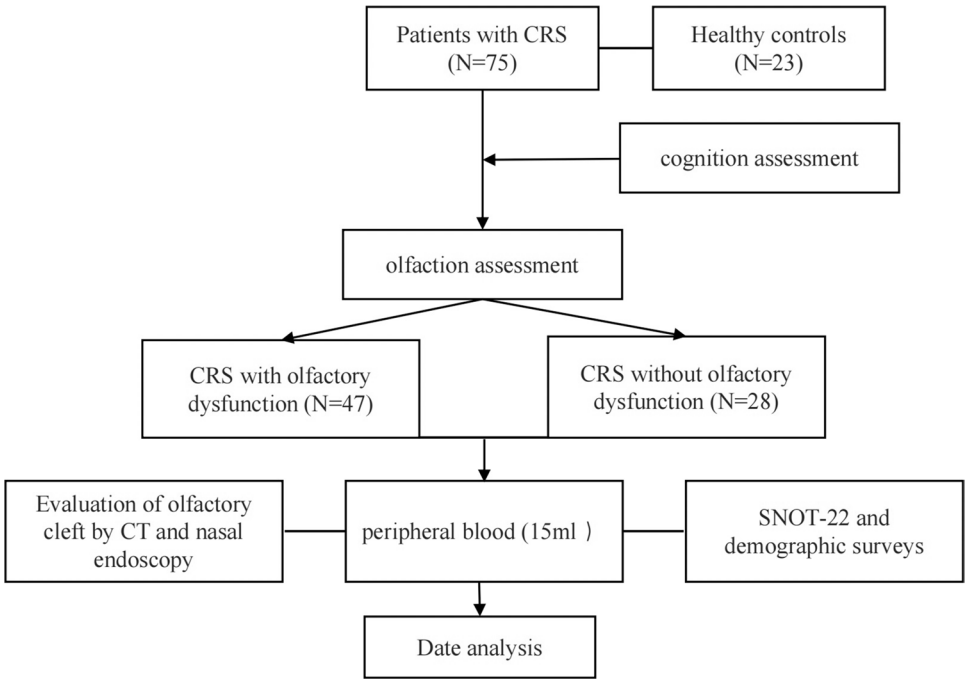

Fig. 1 Flow diagram of the study design. *CRS* chronic rhinosinusitis, *CT* computed tomography, *SNOT-22* 22-item Sino-Nasal Outcome Test

only once, for 3-4 s, the interval between odor presentations was 20–30 s, and the pen should be put about 2 cm from the subject's nostril. Identification and discrimination were scored between 0 and 16, and thresholds between 1 and 16. The results were calculated to a combined score of TDI ranging from 1 to 48. Higher scores indicated better olfactory function. Sniffin' Sticks has been applied in the Chinese population to distinguish between normosmia, hyposmia, and anosmia [27]. In addition, in previous studies, we evaluated patients with healthy and patients with olfactory dysfunction caused by different etiologies in the Chinese population using Sniffer sticks [25, 28, 29]. In this study, we divided the subjects into three groups according to their TDI scores: normosmia (TDI > 30.75), hyposmia (16 < TDI < 30.75), and anosmia (TDI < 15) [30]. In the present study, patients with olfactory dysfunction included patients with hyposmia and anosmia.

Olfactory cleft-specific measures

Sinonasal CT scan and endoscopy were performed in patients with CRS before surgery to determine the severity of the disease. The olfactory cleft is located between the olfactory filum (the anterior plane of the middle turbinate) and the pterygoid sinus. The lateral border of the olfactory cleft is the attachment of the middle and/or superior turbinates, The cribriform plate and 1 cm below the cribriform plate made up the top and bottom of the olfactory cleft. Classification of CRS olfactory cleft turbidity by olfactory cleft CT score, the score of olfactory cleft CT was used as a predictive factor of smell function in chronic rhinosinusitis with nasal polyposis [31], we scored sinus CT scans with the Lund-Mackay Olfactory Cleft Scale (LM-OC) [32]. The olfactory cleft score was the sum of the anterior and posterior olfactory cleft scores, 0 (no turbidity), 1 (25%), 2 (25–50%), 3 (50–75%), and 4 (75–100%) (score range, 0–8), respectively. Evaluation and classification of the pathology of the olfactory cleft with the Olfactory Cleft Endoscopy Scale (OCES) [33]. OCES quantifies the severity of the pathological changes of the olfactory cleft on a scale of 0–2, including discharge, nasal polyps, edema, crusting, and scarring (score range, 0–20). The higher the score on the above staging systems, the more severe the disease. Scoring by doctors with extensive experience in endoscopy.

Statistical analysis

Data was analyzed with SPSS software (SPSS version 26.0, SPSS, Chicago, IL). and Graph Pad Prism (Graph Pad Prism version 9, San Diego, CA, USA). Continuous variable normal distribution test using Shapiro-Walk test. Continuous variables expressed as mean ± standard deviation (SD) or median (with extreme deviation or inter-quartile extreme deviation) indicate normal or non-normal distributions. Comparison of continuous variables using independent samples *t*-test or Mann–Whitney *U*-test (normally distributed or non-normally distributed). These frequency differences between the two groups were assessed by Chi-square (χ^2) test. Spearman rank-order correlations were calculated to evaluate associations between olfaction-specific clinical parameters and cognition scores. Logistic regression analysis was used to assess risk factors associated with cognitive

function in patients with CRS, effect sizes were expressed using regression coefficient β values and their 95% confidence intervals (CIs). The receiver operating characteristic (ROC) curve was used to find the optimal cutoff for each potential factor in patients with CRS with MCI. The area under the curve (AUC) was calculated for each potential factor, and the cutoff value was calculated by the maximum AUC. Bilateral $P < 0.05$ represents a statistically significant difference.

Result

A total of 98 participants were enrolled in this study. Both demographic information to be included and clinical characteristics are presented in Table 1. CRS patients were classified into two different cohorts depending on their olfactory function scores: CRS without olfactory dysfunction ($N = 28$, 37.33%) and CRS with olfactory dysfunction ($N = 47$, 62.67%). The mean age of the heathy controls was 45.04 ± 2.99 (mean ± SD). The median SNOT-22 scores in the control group were 11 (interquartile range: 4–27). The healthy control group had normal olfactory function with median TDI, OD and OI scores were 32.5 (31.5–37.5), 13 (12–14), and 12 (11–14), respectively. The mean OT scores was 8.95 ± 0.63. The median MoCA scores of heathy controls was 27(26–29), and the prevalence of MCI of heathy controls was 8.7%. Significant differences were observed in age, MoCA scores, number of MCI, blood eosinophil count, TDI score, OT score, OD score, OI score, and LM-OC scores between CRS with and without olfactory dysfunction groups (all $P < 0.05$).

Olfactory-specific parameters in CRS with and without olfactory dysfunction

Patients with CRS without olfactory dysfunction had higher olfactory scores (OT, OD, OI, and TDI scores) than patients with CRS with olfactory dysfunction (all $P < 0.05$). Meanwhile, LM-OC scores of patients with CRS without olfactory dysfunction were lower than patients with CRS with olfactory dysfunction ($P = 0.011$). There was no statistical

Table 1 Clinical characteristics of the study participants according to olfactory and cognitive function

Characteristic	CRS with olfactory dysfunction ($N = 47$)	CRS without olfactory dysfunction ($N = 28$)	P value
Age (year)	48.79 ± 1.72	40.07 ± 2.26	< 0.001**
Male, *n* (%)	32 (68.1%)	15 (53.6%)	0.209
Education (year)	12.68 ± 0.41	13.75 ± 0.53	0.227
BMI (kg/m^2)	25.83 ± 0.79	25.47 ± 0.55	0.705
Smoker, *n* (%)	21 (44.68%)	11 (39.29%)	0.648
Alcohol drinker, *n* (%)	22 (46.81%)	11 (39.29%)	0.526
Previous sinus surgery, *n* (%)	2 (4.25%)	3 (10.71%)	0.278
Nasal polyps, *n* (%)	21 (44.68%)	12 (42.86%)	0.535
SNOT-22 scores, median (IQR)	35.23 ± 3.2	31.25 ± 3.26	0.386
MoCA scores, median (IQR)	23 (19–27)	27 (25–29)	< 0.001**
MCI, *n* (%)	30 (63.83%)	9 (32.14%)	< 0.001**
Blood eosinophil count, median (IQR)	0.11 (0.05–0.39)	0.18 (0.08–0.31)	0.019*
Blood basophil count, median (IQR)	0.03 (0.02–0.05)	0.03 (0.02–0.05)	0.706
TDI score, median (IQR)	23.5 (12–27.5)	33.5 (31.13–36)	0.003*
OT score, mean ± SD	3.25 (1–5)	7.5 (6.5–9.38)	< 0.001**
OD score, median (IQR)	8 (4–11)	13 (12–14.75)	< 0.001**
OI score, median (IQR)	12 (11–14)	12.5 (12–13.75)	< 0.001**
OCES, median (IQR)	4 (2–6)	2 (0.25–4)	0.061
LM-OC median (IQR)	0 (0–2)	2 (0–5)	0.011*

CRS chronic rhinosinusitis, *BMI* body mass index, *SNOT-22* 22-item Sino-Nasal Outcome Test, *IQR* interquartile range, *MoCA* Montreal cognitive assessment, *MCI* Mild Cognitive Impairment, *TDI* threshold-discrimination-identification, *OT* olfactory threshold, *OD* olfactory discrimination, *OI* olfactory identification, *OCES* olfactory cleft endoscopy scale, *LM-OC* Lund-Mackay Olfactory Cleft Scale

*$P < 0.05$; **$P < 0.001$

Significant differences in these variables between CRS with and without OD are indicated by superscript. Normally distributed continuous variables are expressed as mean ± SD; non-normally distributed continuous variables are expressed as median (interquartile range). Chi-square test was used to test gender, smoking, and drinking distribution. Independent *t*-test or Mann–Whitney *U* test for comparison between CRS with and without OD

difference in OCES scores was found between the two groups ($P=0.061$) (Table 1).

Cognitive function among patients with CRS with and without olfactory dysfunction

The number of MCI was significantly higher in the CRS with olfactory dysfunction ($N=30$, 63.83%) than in the CRS without olfactory dysfunction ($N=9$, 32.14%) ($P<0.001$). The patients with CRS accompanied by olfactory dysfunction showed statistically lower total MoCA ($P<0.001$), delayed recall ($P<0.001$), attention ($P<0.001$), orientation ($P=0.007$), visuospatial/executive ($P=0.015$), and language ($P=0.033$) scores than patients with CRS without olfactory dysfunction. However, no significant difference in naming and abstraction scores was observed between the two groups ($P>0.05$) (Table 2).

Association of cognitive function with olfaction-specific clinical parameters in patients with CRS

We first analyzed the association between cognitive function and Sniffin' Sticks test results. We found that total MoCA scores were positively correlated with TDI scores ($r=0.549$, $P<0.001$), OD ($r=0.541$, $P<0.001$), OT ($r=0.440$, $P<0.001$), OI ($r=0.382$, $P<0.001$) in patients with CRS. Delayed recall scores were positively correlated with TDI ($r=0.535$, $P<0.001$), OD ($r=0.527$, $P<0.001$), OT ($r=0.491$, $P<0.001$), OI ($r=0.386$, $P=0.001$) in patients with CRS. Attention scores were positively correlated with OD ($r=0.461$, $P<0.001$), TDI ($r=0.427$, $P<0.001$), OT ($r=0.319$, $P=0.005$), and OI scores ($r=0.265$, $P=0.022$). Orientation scores were positively correlated with OI ($r=0.395$, $P<0.001$), TDI ($r=0.369$, $P=0.001$), OD ($r=0.320$, $P=0.005$), and OT scores ($r=0.307$, $P=0.007$). Visuospatial/executive scores were positively correlated with TDI ($r=0.332$, $P=0.004$), OI ($r=0.290$, $P=0.012$), OD ($r=0.280$, $P=0.015$), OT scores ($r=0.248$, $P=0.032$). Language scores were positively correlated with OD ($r=0.291$, $P=0.011$) and TDI ($r=0.254$, $P=0.028$) scores. Both naming and abstraction scores presented no significant correlation with any result of the Sniffin' Sticks test results. We next analyzed the association between cognitive function and the LM-OC score. The LM-OC scores were negatively correlated with attention ($r=-0.381$, $P=0.001$), total MoCA ($r=-0.351$, $P=0.002$), delayed recall ($r=-0.305$, $P=0.009$), language ($r=-0.284$, $P=0.015$), and visuospatial/executive ($r=-0.244$, $P=0.038$) scores. However, the LM-OC scores showed no significant correlation with orientation, naming, and abstraction scores (all $P>0.05$) (Table 3).

Multivariable logistic regression analysis for patients with CRS

To identify possible risk factors for MCI in patients with CRS, we further selected variables for multifactorial logistic regression analysis based on previous studies and clinical background. After adjusting for sex, BMI, age, smoking status, nasal polyps, drinking status, education level, and blood eosinophil count, the OD score was significantly associated with MCI in patients with CRS (odds ratio = 0.792; 95% confidence interval = 0.635–0.988; $P=0.039$) (Table 4).

Predictors in CRS with MCI from ROC analysis

We further determined the cutoff values of each predictor by calculating the maximum AUC area of the ROC curve (Table 5 and Fig. 2). The accuracy of the OD score as a predictor for patients with CRS with cognitive impairment (AUC = 0.722, $P=0.001$) was higher than the OT score (AUC = 0.652, $P=0.024$), whereas the OI score is not available as a predictor for the cognition dysfunction in

Table 2 Comparison of cognition between CRS with and without olfactory dysfunction

Characteristic	CRS with olfactory dysfunction ($N=47$)	CRS without olfactory dysfunction ($N=28$)	P value
MoCA	22.38 ± 0.66	26.93 ± 0.42	< 0.001**
Delayed recall	3.02 ± 0.19	4.18 ± 0.2	< 0.001**
Attention	4.38 ± 0.24	5.68 ± 0.10	< 0.001**
Orientation	5.04 ± 0.19	5.82 ± 0.07	0.007*
Visuospatial/Executive	3.49 ± 0.18	4.18 ± 0.2	0.015*
Language	2.28 ± 0.12	2.68 ± 0.12	0.033*
Naming	2.66 ± 0.10	2.89 ± 0.06	0.148
Abstraction	1.51 ± 0.10	1.5 ± 0.13	0.912

MoCA Montreal cognitive assessment

*$P<0.05$; **$P<0.001$. Significant differences in these variables between CRS with and without OD are indicated by superscript. Independent t test for MoCA

Table 3 Correlation analysis of cognitive function and olfaction-specific parameters in patients with CRS

Parameters	OT		OD		OI		TDI		LM-OC	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Total MoCA	0.440	< 0.001**	0.541	< 0.001**	0.382	< 0.001**	0.549	< 0.001**	− 0.351	0.002*
Delayed recall	0.491	< 0.001**	0.527	< 0.001**	0.386	< 0.001**	0.535	< 0.001**	− 0.305	0.009*
Attention	0.319	0.005*	0.461	< 0.001**	0.265	0.022*	0.427	< 0.001**	− 0.381	0.001*
Orientation	0.307	0.007*	0.320	0.005*	0.395	< 0.001**	0.369	0.001*	− 0.181	0.126
Visuospatial/Executive	0.248	0.032*	0.280	0.015*	0.290	0.012*	0.332	0.004*	− 0.244	0.038*
Language	0.190	0.102	0.291	0.011*	0.086	0.462	0.254	0.028*	− 0.284	0.015*
Naming	0.130	0.265	0.160	0.169	0.143	0.222	0.185	0.112	0.023	0.848
Abstraction	− 0.026	0.828	0.070	0.548	− 0.046	0.696	0.031	0.793	− 0.044	0.714

CRS chronic rhinosinusitis, *OT* olfactory threshold, *OD* olfactory discrimination, *OI* olfactory identification, *TDI* threshold-discrimination-identification, *LM-OC* Lund-Mackay Olfactory Cleft Scale, *MoCA* Montreal cognitive assessment

*$P < 0.05$; **$P < 0.001$. Significant differences in these variables by each group are indicated by superscript

Table 4 Multivariable logistic regression analysis of the predictive factors for CRS with MCI

Variable	*B*	Odds ratio (95%CI)	*P* value
Male	0.176	1.192 (0.352–4.04)	0.778
Smoker	1.047	2.849 (0.371–21.885)	0.314
Drinker	− 1.702	0.182 (0.023–1.434)	0.106
Nasal polyps	0.849	2.338 (0.722–7.573)	0.157
Age	0.013	1.013 (0.965–1.063)	0.607
BMI	0.082	1.085 (0.931–1.265)	0.295
Education	− 0.157	0.855 (0.700–1.045)	0.127
Blood eosinophil count	− 0.256	0.774 (0.044–13.654)	0.861
OT score	− 0.151	0.860 (0.664–1.113)	0.252
OD score	− 0.233	0.792 (0.635–0.988)	0.039*
OI score	0.174	1.190 (0.921–1.538)	0.183

CRS chronic rhinosinusitis, *MCI* Mild Cognitive Impairment, *CI* confidence interval, *BMI* body mass index, *OT* olfactory threshold, *OD* olfactory discrimination, *OI* olfactory identification

*$P < 0.05$. Significant differences in these variables by each group are indicated by superscript

patients with CRS ($P = 0.082$). The OD score with a cutoff point below 11.5 had a higher prediction accuracy (sensitivity = 76.9%, specificity = 61.1%, Youden index = 0.38), and the OI score with a cutoff point below 6.125 had a worse prediction accuracy (sensitivity = 71.8%, specificity = 28.2%, and Youden index = 0.301).

Discussion

The high prevalence of CRS in patients with dementia and cognitive dysfunction in patients with CRS suggests a strong relationship between CRS and cognition [8, 9]. Olfactory dysfunction is not only the main symptom of CRS but also appears in the early stages of neurodegenerative diseases [34–36]. However, whether there is a common mechanism for olfactory function and cognitive function in patients with CRS remains unclear. This is the first study to reveal a tight association between olfaction-specific parameters and cognitive dysfunction in CRS patients. In addition, we determined the predictive role of olfactory discrimination on cognitive dysfunction in patients with CRS. This would help to select which patients are at high risk for cognitive dysfunction and to intervene early in patients.

In this study, we confirmed that patients with CRS had worse cognition scores and a higher prevalence of MCI compared to normal controls, which is consistent with previous

Table 5 Predictors for Patients with CRS With MCI

Predictor	Cutoff	Sensitivity	Specificity	Youden index	AUC	Asymptotic 95% confidence interval		*P* value
						Lower bound	Upper bound	
OD	11.5	0.769	0.611	0.38	0.722	0.603	0.84	0.001*
OT	6.125	0.718	0.282	0.301	0.652	0.527	0.777	0.024*
OI	9.5	0.436	0.564	0.214	0.617	0.489	0.745	0.082

CRS chronic rhinosinusitis, *MCI* Mild Cognitive Impairment, *AUC* area under the receiver operating characteristic curve, *OT* olfactory threshold, *OD* olfactory discrimination, *OI* olfactory identification

*$P < 0.05$. Significant differences in these variables by each group are indicated by superscript

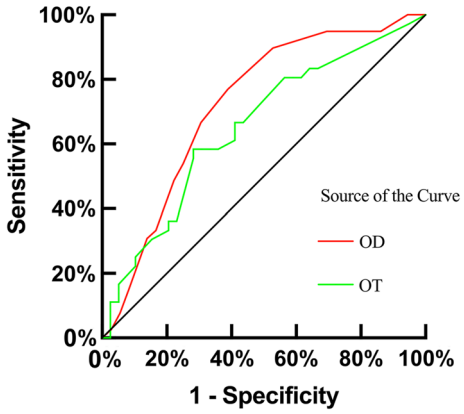

Fig. 2 ROC curve for predictors of MCI in patients with CRS. *ROC* receiver operating characteristic, *MCI* Mild Cognitive Impairment, *CRS* chronic rhinosinusitis, *AUC* area under the receiver operating characteristic curve, *OT* olfactory threshold, *OD* olfactory discrimination

findings [5]. Then, we classified patients with CRS into two groups based on olfactory assessment, CRS without olfactory dysfunction and CRS with olfactory dysfunction. In the present study, we found that the olfactory impairment caused by CRS was characterized by significantly impaired OD and OT scores. The OI scores are relatively preserved, but there was still a statistical difference between the two groups. CRS-related impaired OT scores are caused by the dysfunction of the peripheral olfactory system, resulting in obstruction and edema of the mucosa, preventing odors from passing through the olfactory cleft [37, 38]. Moreover, OD function is related to higher cognitive functions and responds to executive and memory function [38], which indicated that cognitive function may be impaired in CRS patients with olfactory dysfunction.

Our study also found that LM-OC scores were statistically different between the two groups, with higher scores indicating worse olfactory function. LM-OC scores reflect the degree of inflammation and edema in the olfactory cleft. This also suggests that the olfactory dysfunction in CRS is caused by conductive olfactory dysfunction, which is consistent with the previous results [8, 39]. Therefore, we included the LM-OC score as an objective indicator of olfactory function in the assessment of the cognitive function of patients with CRS.

As we expected, the prevalence of MCI was significantly higher in the patients with CRS with olfactory dysfunction than in the patients with CRS without olfactory dysfunction. By comparing the MoCA scores, we found that the patients with CRS with olfactory dysfunction had significantly higher scores than the patients with CRS without olfactory dysfunction. Furthermore, the MoCA scores and olfactory function scores showed a strong positive correlation, indicating that lower olfactory function scores indicated worse cognitive function. Same as previous studies on olfaction and cognition [40, 41], this trend that demonstrated the relationship between olfactory and cognitive function was also present in patients with CRS. Moreover, LM-OC scores showed negative correlation with cognitive function, further indicating that LM-OC scores might be an indicator of cognitive dysfunction. Both subjective CT examination and objective olfactory function examination showed an association between olfaction-specific parameters and cognitive function, which indicates that olfaction-specific parameters can be used as a non-invasive method to measure cognitive function in patients with CRS.

In order to explore the influence of olfaction on the cognitive subdomains of patients with CRS, we compared the cognitive subdomains of two groups. Patients with CRS with olfactory dysfunction had worse cognitive scores in delayed recall, attention, orientation, visuospatial/executive, and language scores. The assessment of olfactory function scores (OT, OD, and OI scores) in CRS patients was positively correlated with the total MoCA scores and each subdomain (delayed recall, attention, orientation, visuospatial/executive, and language scores of MoCA). However, we found no statistical difference between the CRS with and without olfactory dysfunction groups in naming and abstraction scores of MoCA, and olfaction-specific parameters did not correlate with naming and abstraction scores of MoCA. Naming scores are associated with the left and right globus pallidus; abstraction scores are associated with frontal lobe function [42, 43]. We speculate that CRS impairs specific brain regions or brain functional connections (Fc). Jafari et al.[44] analyzed resting-state functional magnetic resonance images of CRS patients and found a significant alteration in Fc in the frontoparietal network, which is an important control center for higher-order neural processing and shows greater activity in complex cognitive tasks. Pengfei et al. performed magnetic resonance imaging scans on CRS patients and found that the volume of olfaction-related gray matter was significantly reduced in CRS patients compared to healthy subjects [45], and the atrophy of gray matter is associated with OD and OI function [46].

In addition, after adjusting for sex, age, BMI, smoking status, nasal polyps, drinking status, and education level, only OD is related to cognitive function. Furthermore, OD has a higher accuracy to predict MCI when compared to OT. When the maximum value of the Youden index was 0.38, the optimal cut-off point for OD was 11.5, with a specificity of 76.9% and a sensitivity of 61.1%. Previous studies have proposed that nasal polyps and pain were highly associated with decreased cognitive function in patients with CRS [47, 48]; This is the first study to explore the predictive significance of OD for MCI in patients with CRS. Several imaging studies have demonstrated that OD is regulated by the hippocampus [49].

The hippocampus was significantly activated during the process of OD [50]. In the functional olfactory cortical network, the hippocampus is crucial in olfactory learning and memory [51]. Furthermore, atrophy of the hippocampal is one of the features of neurodegenerative diseases, and significant hippocampal changes are observed in both Parkinson's disease (PD) and Alzheimer's disease (AD) patients with olfactory impairment. Specifically, reduced hippocampal activity was observed in patients with PD, and the volume of hippocampal and OD scores showed a strong relationship in patients with AD [52, 53]. Different from our results, previous studies have noted that OI scores as a predictor of cognition decline [54–56]. The reason may be explained is that OI impairment is more common in patients with corticobasal dementia, semantic dementia, and frontotemporal dementia [57]. OD has been proven to predict cognitive decline in healthy older individuals [58]. Our results indicate that the predictive effect of OD on cognitive decline is also applicable in patients with CRS.

Our study has some limitations. First, this was a cross-sectional study, the results need to be re-validated in longitudinal and multicenter studies. Second, the sample size was relatively small, the highly selective exclusion criteria exclude many patients. Finally, this study was conducted only on Chinese population. A larger sample size is needed in the future to investigate potential mechanisms of cognitive decline in patients with CRS to reduce the risk of cognitive impairment in patients with CRS. We will perform olfaction-specific clinical parameters and cognition tests in patients with CRS after surgery in our further study.

Conclusion

Our study showed a high association between olfaction-specific clinical parameters and cognitive function in patients with CRS. OD was an independent risk factor for MCI in patients with CRS.

Author contributions All authors have made substantial contributions to the conception, analysis, and interpretation of data in this article, approved the submitted version, and agreed to be personally accountable for our contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which we are not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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