Received: 13 February 2023 | Revised: 25 March 2023 | Accepted: 11 April 2023

DOI: 10.1002/lio2.1061

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Analysis of risk factors affecting olfactory dysfunction in patients with chronic rhinosinusitis: Highlighting the role of metabolic syndrome

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Abstract

Objective: This study aims to evaluate the relationship between chronic sinusitis (CRS) and metabolic syndrome (MS) in a Chinese population and to explore the risk factors for olfactory dysfunction in patients with CRS.

Methods: A total of 387 CRS patients were enrolled. Olfactory function was assessed by the Sniffin' Sticks 12-item test and MS was diagnosed according to the guidelines. Logistic regression analysis was performed on CRS patients to screen independent risk factors of olfactory dysfunction, adjusted for confounding factors.

Results: Among 387 patients, average age of visit and duration of onset were 48.7 years and 1.8 years, respectively. The prevalence of MS was 15.0%. CRS patients with MS were more likely to be older (51.2 vs. 46.8, $p = .004$), predominantly male ($p < .001$) and have a higher proportion of olfactory dysfunction (62.1% vs. 44.1%, $p = .018$) than those without MS. In multivariate logistic regression analysis, MS was associated with olfactory dysfunction in CRS patients (OR: 2.06, 95% CI: 1.14–3.72, $p = .016$). This association remained significant after controlling for confounding factors. In addition, nasal polyps (OR: 13.41, 95% CI: 8.11–22.17, $p < .001$) and allergic rhinitis (OR: 3.16, 95% CI: 1.67–5.99, $p < .001$) were also risk factors for olfactory dysfunction after adjusting for confounding factors.

Conclusions: MS is associated with olfactory dysfunction in patients with CRS. MS, nasal polyps, and allergic rhinitis are risk factors for olfactory dysfunction in CRS patients.

Level of evidence: IV

KEYWORDS
allergic rhinitis, chronic rhinosinusitis, metabolic syndrome, nasal polyps, olfactory disorders

1 | INTRODUCTION

Chronic rhinosinusitis (CRS) is a chronic inflammatory disease of nasal cavity and sinus mucosa, which is characterized by nasal congestion, runny nose, and olfactory dysfunction. The prevalence of CRS has been reported to range from 5% to 14% worldwide[1–4] and the prevalence of CRS in China is about 8%, whose incidence rate tends to increase.[5] Olfactory dysfunction is present in 56%–78% of CRS patients,[6,7] which seriously affects the quality of life of patients and increases the medical burden.[8] Although the specific pathogenesis of olfactory dysfunction in CRS patients has not been clarified, yet, studies have shown that it may be related to aging, immune factors, nasal polyps, genetic factors, and allergy.[9–11] In addition, the effects of metabolic related diseases such as obesity, hypertension, and dyslipidemia on CRS have been increasingly reported in recent years.[12–15]

Metabolic syndrome (MS) refers to the pathological state of human metabolic disorder, which is, respectively, assessed using multiple indices to make the diagnosis: body mass index (BMI), blood pressure, cholesterol levels, high-density lipoprotein (HDL) levels, triglyceride levels, and fasting glucose levels. Several studies have suggested that CRS was closely related to dyslipidemia,[16] obesity, diabetes,[15,17] and hypertension.[18,19] Lee EJ et al. found that CRS was more prevalent in patients with metabolic syndrome, especially those with allergic rhinitis, than in patients without metabolic syndrome.[20] MS was associated with olfactory dysfunction in Korean women in the general population.[21] However, there has been no study to evaluate the direct association between olfactory dysfunction and metabolic syndrome in CRS patients. In this study, we investigated possible risk factors for olfactory dysfunction in Chinese CRS patients and emphasized the role of MS.

2 | MATERIALS AND METHODS

2.1 | Study population

This study is a retrospective review of 387 CRS patients diagnosed at the Department of Otorhinolaryngology, the Third Affiliated Hospital of Soochow University (Changzhou, China) from March 2021 to September 2022. All of them were not infected with COVID-19 and belonged to the Han origin. The study was approved by the Ethics Committee of Third Affiliated Hospital of Soochow University (2022CL070), and informed consent was waived because of anonymous data and no intervention.

2.2 | Inclusion criteria

The diagnosis of CRS was based on EPOS 2012 diagnostic criteria,[22] including clinical symptoms, nasal endoscopy, computed tomography (CT) scan of nasal sinuses, and duration of symptoms more than 12 weeks. Clinical symptoms include nasal congestion, mucinous or mucopurulent runny nose, head and face pain, and olfactory dysfunction. Olfactory function was assessed by the Sniffin' Sticks 12-item test (SST-12) (Burghart Instruments, Wedel, Germany). During the examination, 12 odor-dispensing felt-tip pens were placed in front of the participants' nose for 3 to 4 seconds, in turn, and the participants selected from four visual presentation answers to identify the correct odor. Refusal to answer or "do not know" were coded as incorrect and odor identification score (0–12) was counted according to the number of correctly identified odors. SST-12 score ≥11 was normal and <11 was olfactory dysfunction.[23,24] Nasal polyps were defined by nasal endoscopy and/or CT reports. Recording sites of CRS were included maxillary sinus, sphenoid sinus, ethmoid sinus, and frontal sinus.

Diagnostic criteria of MS have not been completely unified in the world. According to the WHO consultation,[25] joint interim statement of MS[26] and Chinese guideline,[27] MS was defined as the metabolic syndrome risk score (MetS score) of no less than 3, that is, at least three of the following five items must be met:

(1) waist circumference ≥85 cm in women or ≥90 cm in men or BMI ≥28.
(2) fasting blood glucose ≥6.1 mmol/L or diabetes has been diagnosed.
(3) blood pressure level ≥130/85 mmHg or hypertension has been diagnosed.
(4) fasting triglyceride level ≥1.70 mmol/L.
(5) fasting high-density lipoprotein cholesterol level <l.04 mmol/L.

In addition, pre-metabolic syndrome (pre-MS) was defined as MetS score of 2.[28]

2.3 | Exclusion criteria

(1) History of nasal diseases, such as fungal sinusitis, comorbid cystic fibrosis, nasal and sinus tumors, primary ciliary dyskinesia, nasal trauma, and congenital olfactory dysfunction; (2) history of asthma and liver diseases; (3) history of medical treatment or surgery for CRS; and (4) taking glucocorticoids or hepatotoxic drugs.

2.4 | Laboratory testing

Anthropometric parameters and blood pressure were measured by medical staff in the department of otolaryngology. It should be stated that in order to reduce the lack of data, some data of waist circumference were obtained through telephone follow-up. Venous blood was collected on an empty stomach in the early morning by experienced nurses. All these serum biochemical parameters, including triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and fasting blood glucose were measured in the central clinical laboratory of Third Affiliated Hospital of Soochow University by automated analyzers.

2.5 | Possible risk factors for olfactory dysfunction

Based on sociodemographic and personal medical factors identified in previous epidemiological studies, we chose a total of 15 variables, including nasal polyp, gender, age, current smoker, alcohol drinker, allergic rhinitis, diabetes, hypertension, CRS duration, SBP, DBP, HDL, TG, BMI, and MetS score. Nasal polyps, gender, current smokers, drinkers, allergic rhinitis, diabetes, presence of MS or pre-MS, and hypertension were used as categorical variables and CRS duration, SBP, DBP, HDL, TG, BMI, and Mets scores were used as continuous variables. Alcohol drinker was defined as current drinking or stopped drinking <6 months and current smoker was defined as current smoking or stopped smoking <6 months. Allergic rhinitis was identified by allergy testing or medical records.

2.6 | Statistical analyses

Statistical analyses were conducted using the SPSS 24.0 (SPSS Inc., Chicago, IL, United States). The distribution of continuous variables was determined by Kolmogorov–Smirnov test. Continuous variables that conform to normal distribution were represented by mean ± standard deviation, continuous variables that do not conform to normal distribution are represented by median (P_{25}–P_{75}), and categorical data were shown as N (%). The Mann–Whitney *U* test, Student's t-test and Chi-square test were used for comparisons between groups for continuous variables and categorical variables, respectively. Multivariate logistic regression analyses were used to determine the association between olfactory dysfunction and possible risk factors. *P* values <.05 indicated statistical significance.

3 | RESULTS

3.1 | Patient characteristics

A total of 387 CRS patients between March 2021 and September 2022 were included in this study and Table 1 shows their general characteristics. Among them, there were 225 men (58.1%) and 162 women (41.9%). Average age of visit and duration of onset were 48.7 years and 1.8 years respectively. A total of 45.7% of patients presented with olfactory dysfunction. The prevalence of MS and pre-MS were 15.0% (men, 20.9% and women, 6.8%) and 21.2% (men, 21.3% and women, 30.0%) respectively. CRS patients with MS were more likely to be older (51.2 vs. 46.8, $p = .004$), predominantly male ($p < .001$) and have a higher proportion of olfactory dysfunction (62.1% vs. 44.1%, $p = .018$) than those without MS. Both CRS patients with MS and pre-MS had higher BMI, higher waist circumference, elevated triglycerides, elevated blood glucose, elevated blood pressure, and reduced HDL (both $p < .001$). In addition, the prevalence of allergic rhinitis (12.6%, 19.0% vs. 12.2%, $p = .409$) and nasal polyps (48.6%, 58.6% vs. 40.2%, $p = .100$) in patients without MS was not different from that in patients with MS and patients with pre-MS.

TABLE 1 General characteristics of participants.

	CRS participants			
	Without MS	With pre-MS	With MS	*p* value
Male/Female	130/117	48/34	47/11	<.001*
Age of visit, years	46.8 ± 16.3	53.0 ± 14.1	51.2 ± 14.8	.004*
Duration of onset, years	1.6 ± 2.3	2.0 ± 3.2	2.3 ± 4.3	.208
Olfactory dysfunction	109 (44.1%)	32 (39.0%)	36 (62.1%)	.018*
Current smoker	17 (6.9%)	32 (39.0%)	11 (19.0%)	<.001*
Alcohol drinker	14 (5.7%)	10 (12.2%)	9 (15.5%)	.022*
Waist circumference, cm	81.3 ± 4.3	89.0 ± 6.9	94.1 ± 9.1	<.001*
BMI, kg/m^2	22.7 ± 3.8	26.0 ± 3.1	27.2 ± 3.5	<.001*
SBP, mmHg	127.8 ± 14.2	135.0 ± 17.7	138.4 ± 13.0	<.001*
DBP, mmHg	83.0 ± 9.7	87.3 ± 8.1	89.3 ± 9.2	<.001*
Diabetes	22 (8.9%)	39 (47.6%)	29 (50.0%)	<.001*
Hypertension	70 (28.3%)	56 (68.3%)	52 (89.7%)	<.001*
TG, mmol/L	1.0 ± 0.5	1.7 ± 1.0	2.4 ± 1.0	<.001*
HDL, mmol/L	1.4 ± 0.3	1.2 ± 0.2	1.0 ± 0.2	<.001*
Allergic rhinitis	31 (12.6%)	10 (12.2%)	11 (19.0%)	.409
Nasal polyps	120 (48.6%)	33 (40.2%)	34 (58.6%)	.100

Note: Values are expressed as mean ± SE or n (%).
Abbreviations: BMI, Body mass index; CRS, chronic rhinosinusitis; DBP, Diastolic blood pressure; HDL, High-density lipoprotein; MS, metabolic syndrome; SBP, Systolic blood pressure; TG, Triglycerides.
*Significant at $p < .05$.

3.2 | Risk factors of olfactory dysfunction in patients with CRS

According to olfactory function, the baseline characteristics of study participants are shown in Table 2. Male CRS patients with olfactory dysfunction were significantly more likely to be current smokers (20.9% vs. 11.8%, $p = .035$) and have a higher proportion of MS (26.1% vs. 15.5%, $p = .049$), and the course of CRS was longer (2.4 vs. 1.4, $p = .005$). Nasal polyps and allergic rhinitis were significantly associated with olfactory dysfunction in both men and women with olfactory dysfunction. In addition, there was no difference in drinking status, waist circumference, BMI, blood pressure, triglyceride, HDL, presence of diabetes, and pre-MS between patients with olfactory dysfunction and those without olfactory dysfunction.

Table 3 shows the multivariate logistic regression analysis with olfactory dysfunction as dependent variable in CRS patients. The adjusted odds ratio (OR) for olfactory dysfunction was not significant with pre-MS (both $p > .05$). MS, as a categorical variable, was associated with olfactory dysfunction in patients with CRS (Model 1; OR: 2.06, 95% CI: 1.14–3.72, $p = .016$). This association remained significant after controlling for age, gender, duration of onset, smoking status and alcohol intake (Model 2; OR: 2.13, 95% CI: 1.16–3.90, $p = .015$). In addition, nasal polyps (Model 2; OR: 13.41, 95% CI: 8.11–22.17, $p < .001$) and allergic rhinitis (Model 2; OR: 3.16, 95% CI: 1.67–5.99, $p < .001$) were also risk factors of olfactory dysfunction after adjusting for confounding factors.

4 | DISCUSSION

This study indicated that MS were strongly associated with olfactory dysfunction in patients with CRS. Moreover, multivariate logistic analysis determined MS, nasal polyps, and allergic rhinitis as independent risk factors for olfactory dysfunction in CRS patients.

TABLE 2 Univariate analysis of factors potentially associated with olfactory dysfunction.

	Male			Female		
	Olfactory dysfunction	Normal	*p* value	Olfactory dysfunction	Normal	*p* value
Age of visit, years	46.8 ± 17.0	49.1 ± 15.6	.281	47.6 ± 16.5	51.3 ± 14.0	.136
Duration of onset, years	2.4 ± 3.3	1.4 ± 1.8	.005*	1.9 ± 2.1	1.7 ± 3.6	.723
Current smoker	24 (20.9%)	13 (11.8%)	.035*	0	0	NA
Alcohol drinker	14 (12.2%)	18 (16.4%)	.371	0	1 (1.0%)	.433
Waist circumference, cm	86.2 ± 7.0	86.4 ± 6.9	.912	81.1 ± 7.9	82.8 ± 6.7	.439
BMI, kg/m^2	24.5 ± 3.6	24.5 ± 3.4	.981	23.3 ± 3.4	23.7 ± 3.6	.490
SBP, mmHg	133.6 ± 14.9	131.8 ± 14.3	.360	128.0 ± 15.1	128.6 ± 16.8	.827
DBP, mmHg	86.0 ± 9.6	86.4 ± 8.9	.748	83.6 ± 8.5	82.7 ± 10.7	.543
Diabetes	34 (29.6%)	25 (22.7%)	.245	9 (14.5%)	22 (22.0%)	.225
Hypertension	55 (47.8%)	51 (46.4%)	.827	24 (38.7%)	48 (48.0%)	.248
TG, mmol/L	1.5 ± 0.9	1.6 ± 1.0	.457	1.2 ± .8	1.1 ± .5	.320
HDL, mmol/L	1.2 ± 0.3	1.2 ± 0.2	.381	1.4 ± .3	1.4 ± 0.3	.969
Allergic rhinitis	24 (20.9%)	9 (8.2%)	.007*	12 (19.4%)	7 (7.0%)	.032*
Nasal polyps	92 (80.0%)	27 (24.5%)	<.001*	49 (79.0%)	19 (19.0%)	<.001*
Pre-MS	21 (18.3%)	27 (24.5%)	.253	11 (17.7%)	23 (23.0%)	.428
MS	30 (26.1%)	17 (15.5%)	.049*	6 (9.7%)	5 (5.0%)	.287

Note: Values are expressed as mean ± SE or n (%).
*Significant at $p < .05$.

TABLE 3 Multivariate logistic regression analysis with olfactory dysfunction as dependent variable in CRS patients.

	Model 1	*p* value	Model 2	*p* value	Model 3	*p* value
Metabolic syndrome	2.06 (1.14–3.72)	.016*	2.13 (1.16–3.90)	.015*	2.05 (1.10–3.80)	.023*
Allergic rhinitis	3.08 (1.64–5.81)	<.001*	3.16 (1.67–5.99)	<.001*		
Nasal polyps	13.49 (8.24–22.10)	<.001*	13.41 (8.11–22.17)	<.001*		

Note: Values are expressed as odds ratio (95% Confidence interval). Model 1: Adjusted for age and gender. Model 2: Adjusted for age, gender, duration of onset, smoking status and alcohol intake. Model 3: Adjusted for age, gender, duration of onset, smoking status, alcohol intake, allergic rhinitis and nasal polyps.
*Significant at $p < .05$.

In the present study, 45.7% of CRS patients had olfactory dysfunction, which was similar to 56%–78% in the previous study.[6,7] There was one study by Lee et al.[20] reporting that CRS was more common in patients with MS, especially in patients with allergic rhinitis in a Korean population. In recent years, a growing number of studies have confirmed that metabolic risk factors such as obesity, hyperglycemia and dyslipidemia were closely related with olfactory function. Clarhed et al[29] investigated the association between obesity and CRS and found that BMI was a risk factor for the development of chronic rhinosinusitis. Compared with the normal weight group (18.5 ≤ BMI <25), the odds of new-onset CRS was 53% higher in the obese group (BMI ≥30). The olfactory system was recently reported to be connected with the endocrine system,[30,31] and Nam et al.[17] have reported that significant associations between diabetes and CRS with nasal polyps and olfactory dysfunction among patients with CRS in a large national clinical cohort study. Although there were several reports indicating that many people with diabetes had hyposmia, its physiological basis was still unclear.[30,32,33] Wee et al.[16] found that the prevalence of dyslipidemia in CRS patients (26.1%) was significantly higher than that in the control group (20.6%) and correlation between CRS without nasal polyps and dyslipidemia was stronger than CRS with nasal polyps. Having a history of hypertension was an independent risk factor for bleeding after improving endoscopic sinus surgery in patients with CRS, even if taking antihypertensive drugs.[18] olfactory dysfunction inhibited flavor perception and affected food intake.[34] The increase of salt use in some patients with anosmia was presumably to enhance taste perception to compensate for the decrease of taste perception related to loss of smell, which was conducive to the development of hypertension. In our study, hypertension, diabetes, and dyslipidemia, as one of the components of MS, were not directly related to olfactory dysfunction, but the effect was significant after the superposition of factors. We speculate that this may be related to the small sample size of the subjects included in this study, regional and ethnic differences, which may cause selective bias. Therefore, large-scale, randomized, and controlled prospective clinical studies are still needed to further confirm the conclusions of this study.

In the analysis of risk factors of olfactory dysfunction in patients with CRS, nasal polyps, allergic rhinitis, and MS were significant. The mechanism of olfactory dysfunction is not clear and there are two main factors: on the one hand, it is related to conductive olfactory dysfunction, which is caused by nasal mucosal edema and nasal polyps hindering the spread of odor molecules; on the other hand, it is related to olfactory dysfunction of sensory nerve caused by olfactory epithelium or olfactory nerve injury, in which inflammation plays an important role.[35] Litvack et al.[36] showed that olfactory dysfunction in CRS patients were significantly associated with nasal polyposis, smoking, asthma, and age but not with allergic rhinitis. In the type 2/T helper type 2 cell-mediated allergic CRS mouse model, IL-4, IL-5, and IL-13 were increased. These increased cytokines were also implicated in allergic and metabolic conditions, such as allergic rhinitis, obesity, diabetes, and MS,[35,37–39] which can partially explain our results.

To the best of our knowledge, this study is the first study to describe the relationship between MS and olfactory dysfunction in patients with CRS. Hwang et al[21] evaluated the relationship between MS and olfactory dysfunction in the general population and found that olfactory dysfunction was only significantly related to MS in Korean women. In our study, a higher prevalence of MS was observed in male CRS patients with olfactory dysfunction, a phenomenon that was not present in women, similar to the above article. However, after adjusting for gender and other confounding factors, MS was still significantly and positively associated with olfactory dysfunction in CRS patients in multivariate logistic regression analysis. So, we believe that the conclusion is still applicable in women. The strength of this study is that, for the first time, we highlighted the relationship between MS and CRS in a Chinese population and analyzed the risk factors leading to olfactory dysfunction in patients with CRS. However, we acknowledge several limitations in our study. First, this was a retrospective analysis, with some data missing. Although we tried to retrieve relevant data through telephone interviews and so on, a small proportion of data such as waist circumference were still missing. Second, the detailed location of polyps, especially whether there were polyps in olfactory fissure area, was not clearly recorded during the operation. Third, endotypic subtype and the severity of CRS were not measured, which is needed to be assessed in future studies. In addition, whether the risk factors affect the olfactory function for a long time needs to be further confirmed by follow-up.

The associations we found highlight the effect of MS on olfactory dysfunction in patients with CRS. Based on our current research, we cannot draw any conclusion about the causal relationship of the found association nor can we extend the conclusion to the general population. However, in clinical treatment, it may be helpful to pay attention to the relationship between olfactory dysfunction in CRS patients and MS. Improving the status of MS, including hyperglycemia, hypertension, dyslipidemia, and abdominal obesity, may help olfactory dysfunction in CRS patients.

In summary, this was the first study to describe the relationship between MS and olfactory dysfunction in patients with CRS. This study demonstrated that MS, nasal polyps, and allergic rhinitis were risk factors for olfactory dysfunction in CRS patients.

ACKNOWLEDGMENTS

All of the authors are grateful to all of the subjects.

FUNDING INFORMATION

No external funding.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no potential conflict of interests or financial disclosures related to this submission.

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How to cite this article: Zhang L, Wang T, Wang Z, et al. Analysis of risk factors affecting olfactory dysfunction in patients with chronic rhinosinusitis: Highlighting the role of metabolic syndrome. *Laryngoscope Investigative Otolaryngology*. 2023;8(3):615-620. doi:10.1002/lio2.1061