INTRODUCTION

Chronic rhinosinusitis (CRS) with or without nasal polyps (CRSsNP or CRSsNP) is a common chronic condition worldwide.\(^1\) China had CRS prevalence ranging from 4.8% to 9.7% in 2012.\(^2\) Olfactory dysfunction is a common complaint among CRS patients, with a prevalence of 30-60% in them, and is one of the four signs and symptoms to diagnose CRS.\(^1\)\(^,\)\(^3\)\^-\(^5\) Olfactory dysfunction may seriously alter the quality of life (QOL), including safety issues and interpersonal relations, as well as eating habits and nutritional intake.\(^6\) However, standard olfactory tests and managements are limited. Despite the relatively high prevalence and serious influences among patients with CRS, there is a lack of public awareness regarding this problem. The T&T Olfactometer is so called, because it was developed by Toyota and Takagi in 1987 and it aims to determine the detection and recognition thresholds for each of the five odorants (\(\beta\)-phenyl ethyl alcohol, methyl cyclopentenolone, iso-valeric acid, \(\gamma\)-undecalactone, and scatole).\(^7\)

METHODOLOGY

A total of 48 CRS patients with olfactory disorders, including 34 CRSsNP patients and 14 CRSsNP patients were evaluated preoperatively by T&T olfactory test, olfactory VAS test, SNOT-20 score and Lund-Mackay CT score. Outcomes were re-evaluated at 1 month, 3 months and 6 months postoperatively. Results: Both olfactory and SNOT-20 scores showed significant improvement within 6 months in both CRSsNP and CRSsNP groups. Patients with anosmia in T&T test showed the largest degree of improvement. No significant recovery of olfactory dysfunction was observed at 1 month and 3 months in CRSsNP groups postoperative. In CRSsNP, the olfactory scores were correlated with the CT scores significantly (\(r=0.649, p<0.001; r=0.625, p<0.001\)). However, no correlation was found between the SNOT-20 score and olfactory score preoperatively.

Conclusion: Our study has confirmed that the therapeutic effects of ESS on olfactory function last for up to 6 months, particularly in patients with CRSsNP. Although the therapeutic effects plateaued at 3 months postoperatively, the olfactory function continues to recover between 3 and 6 months.


Olfactory dysfunction in CRS is multi-factorial, due to both mechanical obstruction and damage of the olfactory epithelium.\(^8\) Endoscopic sinus surgery (ESS) can remove the obstructions in the nasal cavity and improve the sinus drainage so that gas molecules can reach the olfactory region. ESS for patients with CRS is considered a well-established surgical method in case medical therapy fails,\(^1\) but the olfactory recovery after ESS is still controversial.

Although studies on the relationship between olfactory dysfunction and the quality of life in CRS patients are growing these years, the conclusion is varied. The use of different olfactory assessments and definitions of olfactory improvements have added confusion to the interpretation of the results. Months after the operation are the key period for olfactory recovery. However, the olfactory change pattern after ESS in the short-term and its relationships with CT scores and QOL remain understudied.

The aim of this study was to find the olfactory change patterns of CRS after ESS in the short-term and the differences between CRSsNP and CRSsNP. A secondary aim was to identify the relationships among olfactory dysfunction, CT scores and QOL in subgroups.

METHODOLOGY

A total of 48 CRS patients with olfactory disorders, including 34 CRSsNP patients and 14 CRSsNP...
patients, were collected from December 2014 to January 2016 in Second Hospital of Shandong University. All patients were diagnosed with CRS according to the EPOS 2012 criteria, and experienced an inadequate response to nasal steroid. The general information of participants, including age, gender, current tobacco use, prior sinus surgery, allergic rhinitis and asthma, were recorded when they were enrolled in the research. A CT scan of paranasal sinus was performed preoperative and results were assessed according to the Lund-Mackay scoring system. After surgery, all patients received fluticasone propionate nasal spray for 3 months (400 mcg bid). Patients younger than 18 years with immunodeficiency, cystic fibrosis, head trauma, tumors, endocrine disease, history of mental illness, congenital loss of smell and recent history of upper respiratory tract infections were excluded from the study.

T & T Olfactometer was composed of five basic types of odorants: β-Phenyl ethyl alcohol is the odor of rose and smells light sweet; Methyl cyclopentenolone (Cyclotene) is a burnt and caramel odor; Isovaleric acid is a putrid odor, such as long worn-socks, sweat and fermented soybeans; γ-Undecalactone smells of canned peaches and is very sweet, Skatole is the odor of vegetable garbage, oral or aversive odor. Each odorant is divided into 8 grades (cyclotene includes 7 grades), each grade corresponding to 1 point respectively as -2, -1, 0, 1, 2, 3, 4, 5. The higher the score, the higher is the concentration. The recognition thresholds are recorded, and the average is the final score.

Olfactory dysfunction severities were categorised into 5 classes according to the mean T&T recognition thresholds: class 1 = normosmia (≤1), class 2 = mild (1.1 to 2.5), class 3 = moderate (2.6 to 4.0), class 4 = hyposmia (4.1 to 5.5), and class 5 = anosmia (≥5.5). Postoperative olfactory changes were categorised into 4 classes as cured = recognition thresholds changed to normal; obvious improvement = recovery of 2 points and above; improvement = recovery of 1-2; and invalid = no recovery and even decline.

Visual Analog Scale (VAS) is a 10 cm long ruler, which indicates the degree of patients' subjective olfactory from anosmia (0) on the far left to normosmia (10) on the far right. Patients mobilised the scale according to their own subjective sense of smell to the scale position that matches their olfactory level. The VAS score, which is the distance to the point that patients checked on the line, was calculated. Changes in VAS scores after ESS were calculated as ΔVAS=preoperative VAS-postoperative VAS.

SNOT-20 is a symptom-based rhinosinusitis outcome measure with total of 20 items. Each item records 0 to 5 in the range of 0 to 100. Zero represents no symptoms at all and 5 represents maximal symptoms, with lower scores implying a better quality of life.

Analyses were conducted using SPSS 19.0 statistical software. Kolmogorov-Smirnov test was used to test the data. The changes in the olfactory and the quality of life were analysed by the Wilcoxon test, the results being non-parametric. The relationships among olfactory preoperative, the quality of life preoperative, their changes after surgery, and the CT score were analysed by the Spearman two-tailed bivariate correlations. The differences between the subgroups were analysed by the Mann-Whitney U-test and X2-test (or Fisher's exact test). P ≤0.05 was considered significant for all analyses.

RESULTS

There were 31 men (64.55%) and 17 women (35.45%) with the median age of 39. Four patients (8.33%) suffered from asthma and 15 patients (31.25%) had a history of smoking. Five patients (10.41%) had a history of previous sinus surgery. No significant differences were found between CRSwNP and CRSsNP regarding above clinical characteristics. The median (1st and 3rd quartile) course of disease in CRSwNP was 1.75 (0.38 and 6.25) years, which was significantly longer than CRSsNP 0.30 (0.30 and 1.00). The median (1st and 3rd quartile) preoperative Lund-Mackay CT score was 10.00 (6.00 and 15.75). A significant difference was found in the Lund-Mackay score of CRSwNP as compared to CRSsNP (13 vs. 4.50, p<0.001, Table I). The courses of disease and Lund-Mackay CT scores are non-parametric (p<0.001, Table I). All the data of VAS scores and SNOT-20 scores preoperative and postoperative were non-parametric (all p<0.05). The T&T scores preoperative, 1 month and 6 months postoperative are non-parametric (p<0.001, p=0.04, p=0.04) and the scores at 3 months are parametric (p=0.07).

In total, before ESS, most of the patients (n=18, 37.50%) showed severe olfactory impediment - anosmia. After surgery, 35.42% (n=17), 43.75% (n=21), and 41.67% (n=20) of patients showed mild olfactory impediment at postoperative time points of 1 month, 3 months and 6 months respectively, and occupied the largest population at each time point (Figure 1A-C). Thirty-eight (79.17%) patients showed olfactory improvement at 1 month postoperatively, but it changed to 58.33% (n=28) at 3 month and 62.50% (n=30) at 6 months postoperatively. However, the anosmia group pre-operative showed the most obvious improvement in olfactory function (Figure 1D). A similar tendency of the most obvious improvement was found in CRSwNP (Figure 1E). In CRSsNP, no anosmia patients were found preoperative. After ESS, the olfactory tests in CRSsNP showed that the severity of olfactory acuity impediment in most of these patients changed to normosmia (1 month, 3 months and 6 months postoperative: 64.29%, 57.14% and 71.43% respectively, Figure 1C). The most obvious improvement of...
olfactory was found in the preoperative hyposmia group (Figure 1F).
In all patients, the preoperative median score significantly improved to 1.80 (1.37, 3.73) at 1 month (p<0.001), 2.03 (1.30, 3.10) at 3 months (p<0.001), and 1.40 (0.70, 2.40) at 6 months (p<0.001, Table I). Compared to the score preoperative, no significant changes were found at 1 month and 3 months postoperative in CRSsNP groups (p=0.059, and p=0.626), but there was significant difference between preoperative and the 6-month postoperative score (p<0.05). All scores of preoperative, and the changes of scores at 6 months postoperative in CRSwNP, were significantly higher than in CRSsNP respectively (p<0.05 for all, Table I).

Table I: Descriptive data concerning the enrolled patients, the scores and observed changes at follow-up.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total cohort (n=48)</th>
<th>CRSwNP (n=34)</th>
<th>CRSsNP (n=14)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender [no (%)]</td>
<td>34 (70.83%)</td>
<td>23 (67.65%)</td>
<td>8 (57.14%)</td>
<td>0.522</td>
</tr>
<tr>
<td>Median age, years [1st, 3rd quartile ]</td>
<td>39 (31.52-50)</td>
<td>40 (33.51-50)</td>
<td>31.50 (25.50-58)</td>
<td>0.092</td>
</tr>
<tr>
<td>Asthma [no (%)]</td>
<td>4 (8.33%)</td>
<td>4 (11.76%)</td>
<td>230 (0)</td>
<td>0.307</td>
</tr>
<tr>
<td>Smoking history [no (%)]</td>
<td>15 (31.25%)</td>
<td>13 (38.24%)</td>
<td>2 (14.28%)</td>
<td>0.171</td>
</tr>
<tr>
<td>Prior FESS [no (%)]</td>
<td>5 (10.41%)</td>
<td>5 (14.08%)</td>
<td>1 (7.14%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Median course of disease, years [1st, 3rd quartile ]</td>
<td>1 (0.30-4.57)</td>
<td>1.75 (0.38-6.25)</td>
<td>0.5 (0.30-1)</td>
<td>0.013</td>
</tr>
<tr>
<td>Lund-Mackay CT score [ Median (1st, 3rd quartile )]</td>
<td>10 (6.15,75)</td>
<td>13 (9.75,20)</td>
<td>4.50 (3.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table II: Correlation analysis among the scores and their changes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total cohort</th>
<th>CRSwNP</th>
<th>CRSsNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative T &amp; T olfactory score</td>
<td>r=0.843**,p&lt;0.001</td>
<td>r=0.681**,p&lt;0.001</td>
<td>r=0.583*,p=0.031</td>
</tr>
<tr>
<td>Correlation to VAS olfactory test score preoperative</td>
<td>r=0.817**,p&lt;0.001</td>
<td>r=0.649**,p&lt;0.001</td>
<td>r=0.308,p=0.280</td>
</tr>
<tr>
<td>Correlation to Lund-Mackay CT score preoperative</td>
<td>r=0.757**,p&lt;0.001</td>
<td>r=0.655**,p&lt;0.001</td>
<td>r=0.538*,p=0.05</td>
</tr>
</tbody>
</table>

Table II: Correlation analysis among the scores and their changes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total cohort</th>
<th>CRSwNP</th>
<th>CRSsNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative T &amp; T olfactory score change at 6 months follow-up</td>
<td>r=0.475*,p&lt;0.001</td>
<td>r=0.199,p=0.261</td>
<td>r=0.240,p=0.410</td>
</tr>
<tr>
<td>Correlation to VAS olfactory test score change at 6 months follow-up</td>
<td>r=0.262,p=0.072</td>
<td>r=0.333,p=0.054</td>
<td>r=0.014,p=0.961</td>
</tr>
<tr>
<td>Correlation to Lund-Mackay CT score change at 6 months follow-up</td>
<td>r=0.347*,p=0.016</td>
<td>r=0.405*,p=0.018</td>
<td>r=0.452,p=0.106</td>
</tr>
</tbody>
</table>

The values are expressed as Median (1st and 3rd quartile).
# Significant differences between pre- and 1-month postoperative (p <0.05).
* Significant differences between pre- and 3-month postoperative (p <0.05).
§ Significant differences between pre- and 6-month postoperative (p <0.05)
In CRSwNP, the preoperative median VAS olfactory score 10.00 (8.00, 10.00) significantly improved to 3 (1.75, 7.00) at 1 month (p<0.001), 3 (1.00, 5.50) at 3 months (p<0.001) and 1.00 (1.00, 3.25) at 6 months (p<0.001) after ESS. In CRSsNP, no significantly improvement was found until 6 months after ESS (p=0.630; p=0.207; p=0.025, respectively Table I). The reduction of SNOT-20 scores after ESS was significant in both groups at 3 time points (p<0.05 for all, Table I). No significant differences were found between CRSwNP and CRSsNP.

In both CRSwNP and CRSsNP, preoperative T&T scores were significantly related with VAS olfactory scores (r=0.681, p<0.001; r=0.583, p=0.031). T&T score changes at 6 months follow-up were significantly related with VAS olfactory score changes at 6 months follow-up (r=0.655, p<0.001; r=0.538, p=0.05). Preoperative T & T and VAS scores were found to be significantly correlated with Lund-Mackay CT score in total cohort and CRSwNP (all p<0.05), but not in CRSsNP. VAS olfactory score changes at 6 months follow-up were significantly correlated with the changes in the SNOT-20 score 6 months postoperatively in the total cohort and CRSwNP (r=0.347, p=0.016; r=0.405, p=0.018), but not in CRSsNP. However, in both CRSwNP and CRSsNP, no correlations were found between Lund-Mackay CT score and quality of life (SNOT-20 score), and Lund-Mackay CT score and quality of life improvement 6 months postoperatively (Table II).

**DISCUSSION**

In this study, majority of CRS patients (n=18, 37.50%) suffered from anosmia before ESS. The improvement of olfactory function after ESS was obvious at 1 month and 6 months postoperatively. It is quite interesting that compared to 1 month, the recovery of olfactory dysfunction between 1 and 3 months postoperatively was not obvious. During a short period after surgery, the recovery of nasal ventilation may result in a sensitive state of olfactory cells. Then nasal crusts, mucosal edema, and cyst formation in nasal cavity occur from about 4 weeks to 12 weeks postoperatively. At the same time, the olfactory cells gradually adapt and decrease their sensitivity. This recovery procedure after surgery might explain the plateau of olfactory recovery at 3 months postoperatively. Subsequently, with the continuous diminishment of inflammatory status of the cavity, nasal epithelium remodels. As a result, olfactory function experienced a stable improvement in tested indices up to 6 months follow-up. Levy et al. evaluated olfactory outcomes among CRS patients at 6 months, 12 months, and 18 months postoperatively, noting that overall improvement persisted between 6 months and 18 months after ESS for most patient subgroups. Thus, 3 months after operation are the key period for olfactory recovery. Both the patients and doctors should pay more attention to the management of this initial improvement.

This study demonstrates that olfactory function is differentially affected between patients within subgroups of CRS, which coincides with a previous investigation by Alt et al. In the present study, olfactory dysfunction in CRSwNP was much greater than in CRSsNP. It seems that a high degree of olfactory dysfunction may predict postoperative success in terms of olfactory function. Mechanical obstruction and the inflammation injury of olfactory epithelium were shown as two main reasons for the olfactory disorder in CRS patients. Both of the two factors are important in reducing the olfactory acuity in
CRSwNP, while in CRSsNP mechanical obstruction plays a limited role. ESS physically removes polyps, increases airflow that reaches the olfactory cleft and diminishes the overall inflammatory state of the sinonasal mucosa. Thus, most patients have a large degree of improvement in the sense of smell within a short period after ESS, especially CRSwNP patients.

Some studies have shown the CT score was correlated to olfactory dysfunction in CRS.\textsuperscript{3,15} Olfactory cleft opacification on CT scan was the most important indicator for olfactory dysfunction.\textsuperscript{16} In this study, the olfactory was significantly correlated with the Lund-Mackay CT score in the total cohort as well as in CRSwNP. However, there was no correlation in the CRSsNP group, which increased the likelihood of perfect confounding by polyp status rather than a true association between Lund-Mackay CT score and olfactory dysfunction. In both CRSwNP and CRSsNP, no relationships were found between the changes of the olfactory test score 6 month postoperatively and CT score. Thus, the preoperative CT might not be able to predict the postoperative olfactory improvement.

As different studies utilised different methods to measure the QOL and different methods contain different contents, some studies documented that olfactory impairment had a negative impact on many aspects of daily life,\textsuperscript{6,17,18} while other studies showed that the olfactory function did not correlate with QOL measures.\textsuperscript{15} In this study, the SNOT-20 was used to measure the QOL of the patient, and the results showed that no correlation between olfactory function and SNOT-20 score. This may be because SNOT-20 did not have specific questions regarding olfactory symptoms and limitation existed in assessing the quality of life associated with the sense of smell. As a result, a better testing method should be developed and unified. Both the QOL and the change of it after ESS had no relationship with the Lund-Mackay CT score in our study, which coincides with some previous investigations where weak or no association were found between Lund-Mackay CT score and the tested health-related quality of life measures.\textsuperscript{19,20} Although a recent study by Henrik Lind showed positive correlation between the Lund-Mackay CT score and SNOT-22 results in CRSwNP, the relationship was moderate to weak,\textsuperscript{21} Thus, associations between the QOL and the objective outcome measures of CRS remain elusive, and more studies are needed to reveal this knowledge.

**CONCLUSION**

Olfactory dysfunction is more severe in CRSwNP group. Therapeutic effects of ESS on olfactory function and QOL last for up to 6 months, particularly in patients with CRSwNP. Although the therapeutic effects plateaued at 3 months postoperatively, the olfactory function continues to recover between 3 and 6 months. However, the small CRSsNP group size and a relatively short follow-up were limitations of the study. Further studies are required to maintain a favourable long-term olfactory condition.

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**REFERENCES**


