

Nasal polyp load determines the recovery of olfaction after surgery for chronic rhinosinusitis*

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Abstract

Background: Chronic rhinosinusitis (CRS) is typically accompanied by impairment of olfaction. Despite of this, until today the efficacy of endonasal sinus surgery (ESS) in terms of olfactory function is still unclear. So far it is known that patients with nasal polyps are most likely to experience post-operative recovery. Within the present study we investigated the sense of smell and other parameters of impairment in CRS before and after ESS in relation to the degree of nasal polyposis, determined with the nasal endoscopic Lildholdt-score.

Methods: Patients with different degrees of severity of nasal polyposis were included. Olfactory function was assessed for odor thresholds [T], odor discrimination [D] and odor identification [I] and the changes of these parameters were investigated postoperatively.

Results: For 72 patients baseline measures were available and in 47 patients, postoperative changes were described. There was a correlation between olfactory scores and nasal anatomy/polyposis scores (Lildholdt scores, Lund-Mackay CT score), rated nasal health, and nasal quality of life (sinonasal outcome test). Three months after surgery the average TDI-Score improved by 3.1 points with 30% of patients showing significant clinical improvement. Patients with severe polyposis (Lildholdt score of 5 or 6) benefited most in terms of olfaction. Other significant prognostic indicators of a postoperative increase of olfactory scores included younger age, low pre-operative TDI-scores and high CT-scores.

Conclusions: This study shows that not only the presence of polyps in CRS, but also the degree of nasal polyposis - measured by a grading system - predicts the results in olfactory test results. Additionally, the degree of recovery of olfaction after ESS seems to be most relevant in patients with high polyp scores.

Key words: Sniffin´ Sticks, sense of smell, nasal polyps, polyp-score, CRSwNP

Introduction

Chronic rhinosinusitis is a common disease with a prevalence of 5-12% in the USA and Europe^(1,2). CRS is accompanied by a distinct reduction in quality of life, particularly nasal obstruction, nasal discharge and decreased sense of smell. Phenotypically two types of CRS are described, chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP)⁽³⁾. Especially olfaction is more severely affected in the CRSwNP phenotype^(4,5). Apart from topical nasal and

systemic steroids, endonasal sinus surgery (ESS) is a treatment option, which has shown to improve symptoms, quality of life and endoscopy scores^(6,7).

The effect of sinus surgery on olfaction is still not fully understood, although some reviews and meta-analyses have been published in recent years^(8,9). The results from studies looking at the benefit of sinus surgery for olfaction in patients with CRSsNP are inconsistent^(10,11). In patients with CRSwNP, however, more studies using sophisticated tests for olfaction had similar

findings⁽¹²⁻¹⁴⁾. It has been confirmed that the best chance of recovery of the sense of smell after sinus surgery can be seen in patients with CRSwNP who had their first surgery and who were anosmic prior to operation^(15,16).

Especially in CRSwNP the recurrence of polyps is increased if patients additionally have type II disease like asthma or non-erosive reflux disorder as co-morbidity⁽¹⁷⁾. Here new medical treatment options by so-called biologicals are available today⁽¹⁸⁻²⁰⁾. An effect on the sense of smell has been reported for some therapeutic constellations⁽²¹⁾.

Clinically the term CRSwNP has been further refined in the way that not only the presence of nasal polyps is described, but a grading system for nasal polyposis has been established⁽²²⁾. A similar grading system is frequently used in studies for biological treatment of CRSwNP. In studies evaluating the effect of nasal surgery on olfaction a specific classification of nasal polyposis is not used so far, and therefore results are difficult to compare. Especially in studies on the impact of nasal polyps on olfaction all kinds of degrees of polyposis are included and not further divided^(10,11,23,24). Hence, to examine the potential effect of sinus surgery in CRSwNP on the sense of smell, prospective studies are needed using a sophisticated polyp grading system in combination with validated psychophysical testing methods. One such olfactory test battery is the "Sniffin' Sticks" which cover various domains of olfactory function including odor threshold, discrimination and identification^(25,26).

The aim of this study was to investigate the preoperative olfactory measures in CRS patients in detail using different scoring methods and describe changes of olfaction after ESS with a particular focus on the graded severity of nasal polyposis.

Materials and methods

Study design

The prospective study was conducted in accordance with the Declaration of Helsinki on Biomedical Studies Involving Human Subjects. It was approved by the Ethics committee at the Dresden University Hospital (approval number EK14502017). All participants gave written informed consent.

Setting

The cohort included patients who were preparing for endoscopic sinus surgery at the Department of Otorhinolaryngology at the TU Dresden. Measurements took place between January 2019 and January 2021. All patient underwent prior conservative treatment including topical nasal steroids that did not resolve the complaints. After surgery for all patients saline rinses were recommended and all participants continued a topical nasal steroid treatment. After three months, a re-assessment took place.

Participants

Inclusion criteria were patients with bilateral sinus disease for more than 3 months despite conservative treatment, age 18 years and older. Primary cases and also patients with recurrent disease after prior surgeries were included. Exclusion criteria were pregnancy, signs of neurodegenerative disorders such as Parkinson's or Alzheimer's disease or other disorders that are strongly associated with olfactory loss, e.g., advanced renal dysfunction or major head trauma in the past. All patients were screened for the presence of allergies to inhalant allergens verified by allergy testing (skin PRICK testing and/ or specific blood IgE).

Variables and measurements

Polyp-score

The endonasal polyp-score was determined by the classification of Lildholdt⁽²²⁾ for each side by nasal endoscopy of an experienced specialist. An absence of nasal polyps is scored as 0, small polyps not reaching the upper edge of the inferior turbinate scores 1. Medium polyps between the upper and the lower edges of the inferior turbinate are graded as 2. Large polyps reaching the lower edge of the inferior turbinate is given a score of 3. The total score is calculated by adding up the two scores for each side with a maximum of 6. A total score of 1 or 2 was regarded as mild polyposis, a polyp score of 3 or 4 was regarded as moderate polyposis and a score of 5 or 6 was regarded as severe polyposis.

Olfactory testing

Olfactory function was quantified using an established clinical test ("Sniffin' Sticks", Burghart Instruments, Wedel, Germany)⁽²⁵⁻²⁸⁾, which evaluated three sensory dimensions of odors comprising olfactory threshold (to phenylethyl ethanol), odor discrimination (16 pairs of odors) and odor identification (16 odors). The olfactory functional diagnosis was obtained from the sum of scores for Threshold, Discrimination and Identification (TDI) subtests, with a range between 1 and 48 points and allows to categorise subjects as normosmic (sum score > 30.5 points), hyposmic (16.5 - 30.5 points), and functionally anosmic (< 16.5 points), based on normative scores obtained in more than 9,000 healthy subjects⁽²⁹⁾. Studies on the minimal clinical important difference (MCID) for changes of the TDI-score are available.

Assessment of the quality of life

As a disease-specific measure of the patients' quality of life, the Sino-Nasal Outcome Test (SNOT)-22 questionnaire^(30,31) was used to quantify sinonasal symptoms. It consists of 22 questions of CRS-related items scored from 0 to 5 (total score range 0-110, higher scores represent worse symptoms), which evaluates the severity of complaints that patients have been experiencing over the past weeks due to CRS. Scores of 40 or more are considered representing a severe impairment⁽²⁾.

One item of the SNOT-22 is a question about impairment in

Table 1. Demographic basic data of all patients included in this study with CRS and the subgroup of patients with pre- and post-operative results.

	Pre-operative group	operative group
n	72	47
Age (years)	51.1	50.7
female	29 (40%)	20 (43%)
male	43 (60%)	27 (58%)
atopy	32 (44%)	22 (47%)
asthma	25 (35%)	19 (40%)
NERD	10 (14%)	5 (11%)
previous sinus surgery	16 (22%)	9 (19%)
SNOT-22	27.3	26.6
VAS	5.31	5.40
Lund Mackay-Score	10.94	11.66
Lildholdt-Score	2.5	2.53
no polyposis	3 (4%)	0
mild polyposis	42 (58%)	29 (62%)
moderate polyposis	16 (22%)	11 (23%)
severe polyposis	11 (15%)	7 (15%)
TDI-Score	24.8	24.3
Threshold	4.9	4.3
Discrimination	9.9	9.7
Identification	10.5	10.3
Normosmia	24 (33%)	14 (30%)
Hyposmia	30 (42%)	10 (43%)
Anosmia	18 (25%)	13 (28%)

smell and taste and has been used separately in this study as subjective evaluation of the sense of smell (0= no problem, 5=as bad as it can be).

Visual Analogue Scale

A recommended method for subjective assessment of severity of nasal symptoms in CRS is the use of a visual analogue scale (VAS) recorded by the patient on a 10cm line giving a score on a measurable continuum of 0 to 10cm⁽³²⁾. A range from 0-3 cm would indicate mild symptoms, from >3 to 7 of moderate symptoms and >7 severe symptoms.

Follow-up

After sinus surgery, all patients used nasal washings and topical nasal steroids. Patients were followed-up 3 months after the operation and all measurements were repeated, including nasal endoscopy.

As primary outcome criterion the impact of the polyp-score on the baseline TDI-score was determined. Secondary outcome

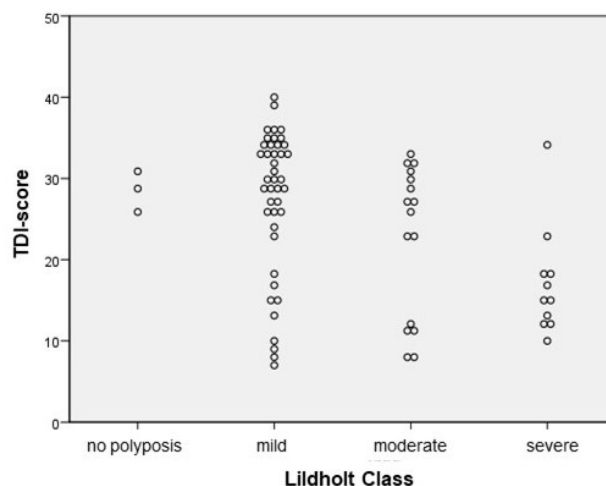


Figure 1. Individual TDI-results in the pre-operative group (n=72) depending on the Lildholdt-class (no polyps; mild polyposis with endoscopic Lildholdt scores of 1 or 2; moderate polyposis with Lildholdt scores 3 or 4; severe polyposis with Lildholdt score of 5 or 6).

measure was the change of TDI-score 3 months after surgery depending on the polyp score.

Statistics

All analyses were performed using the IBM SPSS Statistics, Version 27.0 software system (IBM, Germany). Histograms and skewness were used to evaluate normal-distribution. Mean values were computed \pm standard deviations. In normally distributed values a T-test was used for statistical analysis. Spearman correlations were computed. The significance level was set at $p < 0.05$. Other explorative analyses were performed wherever deemed appropriate. In these cases, p values are given for descriptive reasons only. Influences of different parameters on olfaction preoperatively were evaluated using the Mann-Whitney U test. Kruskal-Wallis-tests were performed in independent samples. Multivariate regression was used to identify influencing factors for baseline measures and changes of smell test results.

Results

Baseline function

For the analysis of baseline olfactory function, the data of 72 patients (43 men, 29 women; aged 23-79 years, 51.1 ± 14.6 years) could be evaluated. The demographics are shown in Table 1. The mean pre-operative TDI score was 24.8 points, with a mean threshold of 4.5 points, a mean discrimination score of 9.9 points and a mean identification score of 10.5 points. Women scored higher compared to men for all olfactory tests ($p < 0.05$). Using a multivariate regression model, other factors for a low TDI Score were high CT-score ($p < 0.001$), and a high Lildholdt-score ($p = 0.019$).

Regarding the primary outcome measure, the Lildholdt group-

Table 2. Significant correlations ($p \leq 0.05$, Spearman) between endoscopic polyp score (Lildholdt score) and TDI-total score and subscores, CT-score and patient rated outcome measures of all patients included in this study at baseline.

	Lildholdt score
TDI-Score	$r = 0.54$
Threshold	$r = 0.62$
Discrimination	$r = 0.35$
Identification	$r = 0.49$
Lund Mackay-CT-Score	$r = 0.54$
VAS	$r = 0.47$
SNOT-22	$r = 0.30$
Item "Smell" in SNOT-22	$r = 0.46$

ping revealed that the average TDI score was 28.8 in the group without polyps, 27.4 points in the group with mild polyposis, 22.6 points in the group with moderate polyposis and 17.1 in the group with severe polyposis (Figure 1) ($p=0.004$). For the three olfactory tests, a significant difference was only found for threshold ($p<0.001$) and identification ($p=0.026$), but not for odor discrimination ($p=0.062$).

Correlations between the Lildholdt score and other parameter are displayed in Table 2. Of note, the Lildholdt score showed significant correlations with the TDI-score and its subtests, with thresholds showing the highest correlation.

Results after surgery

For the analysis of changes in olfaction after sinus surgery, a full data set of 47 patients was available (27 men, 20 women; aged 28-77 years, 50.7 ± 14.0 years). Here, only data of patients with a Lildholdt-score of 1 or more were included. Therefore the three patients without nasal polyps were excluded. The extend of the surgery was been adapted to the individual degree of the disease. In most cases bilateral functional endoscopy surgery or extended endoscopic surgery has been performed. Lothrop procedures were not included. Of the included 47 patients, nine patients had previous sinus surgery; the maximum number of previous sinus surgeries was 2 in 3 patients. The mean Lund-Mackay-score in this group was 11.7 points, 24 patients showed scores below 12 points, 23 above.

The surgery group showed an average increase in TDI-score of $3.1 (\pm 8.1 \text{ SD})$, ranging from -24.3 to +27.4 ($p < 0.008$, Wilcoxon Test) with an average increase of $0.9 (\pm 2.7)$, $1.4 (\pm 3.6)$, and $0.8 (\pm 3.4)$ for T, D, and I, respectively. These changes from baseline were significant for TDI ($p=0.012$), T ($p=0.026$), and D ($p=0.011$), but not for I ($p=0.12$).

Regarding the secondary outcome measure, the mean impro-

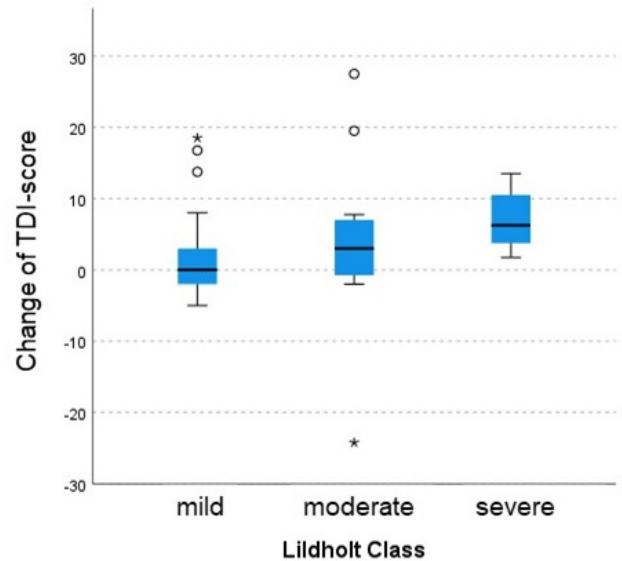


Figure 2. Change of TDI-score after ESS depending on the Lildholdt-score prior to surgery. ($p=0.032$, Kruskal-Wallis-Test for independent samples). Dots represent mild outlier, the asterisks severe outlier (> 3 times interquartile range).

vement of the TDI score in the group of mild polyposis was 1.8 points ($n=29$; $p=0.12$), in the moderate polyposis group the mean increase was 3.8 points ($n=11$; $p=0.36$) and in the group with severe polyposis the increase was 7.1 points ($n=7$; $p=0.005$) (Table 3 and Figure 2). This result could be supported in a linear regression analysis, where the Lildholdt-score contributed significantly to the post-operative change of TDI-score ($p=0.048$). Baseline TDI-score also turned out to be a strong predictor for TDI-improvement after surgery ($p<0.001$).

Additionally, changes in TDI-score were more likely to be reached if the patients were younger, and if the patients had a higher VAS. Other factors like previous surgery or asthma did not show an impact on the change of TDI score in the model.

With regard to the MCID for the Sniffin' Sticks TDI-score⁽³⁶⁾, approximately 2/3 ($n=31$) showed no change (improvement of less than 5.5 or decrease of less than 5.5 points), approximately 1/3 ($n=15$) improved by more than 5.5 points and 1 of the 47 patients decreased by 24 points.

When looking at the olfactory group, before surgery, 14 patients showed normosmia (30%), 20 patients were hyposmic (42%) and 13 patients had functional anosmia (28%). Three months after surgery 21 patients were normosmic (45%), 21 patients were hyposmic (45%) and 5 patients were anosmic (10%). Eighteen patients showed an increase in olfaction (from hyposmia to normosmia or anosmia to hyposmia or normosmia), 25 patients stayed in the same group and 4 patients decreased in the diagnostic group (from normosmia to hyposmia/anosmia or

Table 3. Changes of the olfactory test results in the Sniffin´ Sticks test of 47 ESS-patients before and after surgery depending on the Lindholdt-class.

	Before surgery				After surgery				P-value
	T	D	I	TDI	T	D	I	TDI	
Mild polyposis	5.4	10.6	11.6	27.5	6.0	11.4	12.0	29.4	p=0.12
Moderate polyposis	3.0	8.8	8.4	20.2	4.2	10.2	9.6	24.0	p=0.36
Severe polyposis	2.0	7.3	8.3	17.6	3.7	11.0	10.0	24.7	p=0.005

Table 4. Changes of VAS (visual analogue scale)-score, SNOT (Sino-Nasal Outcome Test)-22 score and class of olfaction in the group with pre- and post-operative assessment (n=47).

	Before surgery	After surgery	p-value
SNOT-22	26.6	16.7	p<0.001
VAS	5.4	3.8	p<0.001
Anosmia	13 (28%)	5 (10%)	
Hyposmia	20 (42%)	21 (45%)	
Normosmia	14 (30%)	21 (45%)	

hyposmia to anosmia).

The changes in the VAS-score, SNOT-22 score and class of olfaction are summarised in Table 4.

Asthma, NSAID-exacerbated respiratory disease (NERD) or allergy were not associated with a change in olfactory function ($p>0.05$).

Other parameter like the SNOT-22 score improved by an average 9.9 points (from 26.6 to 16.7, $p < 0.001$). The correlation between the item "smell function" in the SNOT-22 questionnaire correlated before ($r=0.64$, $p<0.001$) and after surgery ($r=0.36$, $p<0.013$) with the TDI-scores. The changes of TDI-score and changes of item smell function after 3 months of surgery showed a low correlation as well ($r=-0.30$, $p=0.042$).

If only patients with initially decreased olfaction were regarded, approximately 50% showed a clinically significant increase in TDI-score or an increase in the olfactory group.

Discussion

Whereas recent reports on the outcome of olfaction after sinus surgery only made a distinction between CRSsNP and CRSwNP, the present study shows that the degree of polyp formation has a major effect on baseline olfaction and the recovery of olfaction after sinus surgery.

The CRS-population described in this study was comprised mostly of CRSwNP patients. This is consistent with other studies using the Sniffin´ Sticks test battery for investigating changes in olfaction after ESS^(13,14,16,37-39). Only 3 patients in this study

exhibited CRSsNP. In terms of demographic factors, the patient group was comparable to other studies with half of patients showing atopy, with asthma as co-morbidity in one third and NERD in 15% of all included subjects. Unlike previous studies, however, the extent of polyposis has been classified. Most of the patients ($n=42$) in the present study were assigned to a group of mild polyposis referring to the Lindholdt-score (58%), 16 patients (22%) showed a moderate extent of nasal polyps and 15% showed a severe polyposis. This explains the finding that the mean olfactory score of the Sniffin´ Sticks TDI-test was higher in contrast to other studies⁽²³⁾. Also, the number of patients with a relevant impairment of the sense of smell was lower than described by others where either impairment rates $>70%$ ^(15,16,37,39) or even 100%⁽¹³⁾ had been reported. One reason seems to be the relatively large number of patients with mild polyposis as a proxy for less severe disease and lower degree of inflammatory load. This idea is supported by the low number of revision cases of 20% and the relatively low Lund-Mackay-score in comparison to other studies⁽⁴⁰⁾.

The differentiation of polyp score using the Lindholdt-score allowed to assess possible differences in olfactory recovery following ESS. The follow-up period of 3 months is commonly used as an interval between surgery and re-assessment⁽³⁸⁾. Despite a relatively mild impairment of the sense of smell prior to surgery in most of the participants of this study, a significant improvement could be shown in this group of patients. This improvement correlated well with other reports⁽⁹⁾. The question about the clinical relevance of an improvement of 2 or 4 points (mild and moderate polyposis group, respectively) in the post operative TDI-score is valid, because the MCID for the extended Sniffin´ Sticks battery is regarded to be more than 5 points⁽³⁶⁾. A clinical relevance can be judged by the fact that the subjective estimation of the sense of smell correlated well with the Sniffin´ Sticks TDI-score as well as the changes of these two parameters after surgery. Therefore it can be estimated that patients are aware of the improvement of olfaction.

It is commonly assumed that sinus surgery is most effective in patients with polyps that are suffering from anosmia. The present study clearly confirmed this assumption, based on the detailed quantification of both olfactory function and nasal polyposis using validated and reliable tools. As described earlier, si-

nus surgery also may result in a deterioration of olfaction. In our group one patient (a 58 year old female with revision surgery and a preoperative Lildholdt score of 4 and a TDI score of 33.25) exhibited a strong decrease of 24 TDI points after surgery, even without polyp-recurrence. The reason for this remains unclear⁽⁸⁾.

Limitations of the study

This study has limitations despite its prospective design. The patients included in the baseline evaluation showed only limited disease in the Lund-Mackay-Score and rather lower nasal polyp-scores with almost 2/3 showing a Lildholdt-score of 2 or lower. These factors lead to relatively good results in the preoperative TDI-Scores with only 25% showing anosmia and more than 30% showing normosmia. Therefore, this cohort may not represent a typical group of patients qualifying for sinus surgery. On the other hand, this broad distribution of nasal polyp scores made it possible to describe differences including low polyp scores. Additionally, the drop-out rate of patients who were analysed at baseline and those with postoperative results was relatively high. Still significant results were found and the two groups, drop-outs and patients staying in the study, did not differ significantly concerning baseline measures (Table 1).

Conclusion

This study helps to close a gap in investigating the potential of restoring olfaction after endonasal sinus surgery in less pronounced CRSwNP, as most patients included into this investigation showed minor polyposis and were not completely impaired in terms of their sense of smell. Hence, they exhibited mostly hyposmia or even normosmia prior to surgery. Despite of this precondition an improvement in the sense of smell is possible in all groups after sinus surgery. Nevertheless, the results clearly showed that the higher the degree of pre-operative polyposis, the higher the mean increase of olfaction after ESS.

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Authorship contribution

All authors were involved in the design, delivery and analysis of the study, and have written and edited this manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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