

Improvement of Olfactory Function for Quality of Life Recovery

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Objectives/Hypothesis: To explore quality of life (QoL) improvement after treatment of patients with chronic olfactory disorders; and to correlate QoL with olfactory rehabilitation and evaluate olfactory improvement values over which QoL outcomes are significantly recovered.

Study Design: Prospective clinical study.

Methods: Eighty-nine patients following endoscopic sinus surgery for chronic rhinosinusitis (CRS) and immunotherapy for allergic rhinitis (AR) were studied. Olfactory function was evaluated using Sniffin' Sticks test pre-and 12 months after treatment. All patients completed six validated QoL questionnaires either specific for olfaction (Questionnaire of Olfactory Deficits-QOD) and for assessing mental health (Zung Anxiety Scale, State-Trait Anxiety Inventory, Zung Depression Scale, Beck Depression Inventory), or generic one (Short Form-36).

Results: Significant improvement (all $P < 0.001$) of olfactory function by 27.4% in total cohort (AR: 10.4%, $P = 0.004$; CRS: 39.9%, $P < 0.001$), expressed by the combined Threshold-Discrimination-Identification (TDI) score-and of all QoL questionnaires scores (all $P < 0.01$) as well, was observed after treatment. There was a positive correlation between olfactory recovery and improvement of patients' QoL. ROC analysis revealed that an increase in the TDI score by 3.50 points in AR and 4.75 points in CRS was necessary for a clinically significant improvement in all QoL questionnaires results.

Conclusions: QoL and mental health of patients suffering from chronic sinonasal diseases are totally recovered after treatment, presenting a direct positive relationship with smell improvement. An increase of olfactory function by 3.50 points for AR and 4.75 points for CRS might be considered the cutoff point for patients' QoL significant recovery.

Key Words: Olfactory function, quality of life, chronic rhinosinusitis, allergic rhinitis, endoscopic sinus surgery, sniffin' sticks.

Level of Evidence: 4.

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INTRODUCTION

Chronic rhinosinusitis (CRS) and allergic rhinitis (AR) are the most common chronic associated sinonasal diseases^{1,2} and of the most common causes of olfactory disorders.³ Olfactory dysfunction is a major symptom among these patients,¹⁻⁴ closely related to mental health (MH) and quality of life (QoL).^{5,6} There are studies to describe endoscopic sinus surgery (ESS) as the gold standard in the treatment of CRS⁷⁻¹⁵ and immunotherapy of AR¹⁶⁻²⁰ for symptoms resolution, even for olfactory function and QoL; however, the issue of olfaction/QoL correlations after appropriate treatment has not been adequately discussed in literature. Moreover, there is no data available to provide the improvement

values of olfactory function that lead to clinically significant QoL recovery in CRS and AR diseases and needs to be explored. The clinical relevance is that this data may enable otorhinolaryngologists to answer their patients' questions about the anticipated benefit for their QoL after treatment and how it is correlated to olfactory function. This may also support clinical decisions on the holistic management of patients suffering from chronic sinonasal diseases, such as CRS and AR. The use of standardized olfactory tests and validated psychometric instruments opens new horizons for evaluating the olfaction/QoL associations during treatment.

The aims of our study were consequently: 1) to prospectively evaluate QoL posttreatment outcomes and compare them to the results of healthy subjects, 2) to address the latter's relationship with olfactory recovery rates, and finally 3) to determine quantitatively which are the improvement values of olfactory function over which patients' QoL outcomes are significantly recovered.

MATERIALS AND METHODS

Eighty-nine patients suffering from olfactory deficits due to chronic rhinosinusitis [either with nasal polyps (NP): CRSwNP, or without NP: CRSsNP] and allergic rhinitis were studied between September 2009 and August 2012; 19 patients were lost to follow-up. Thirty healthy subjects with no evidence

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TABLE I.
Frequency of Treatment Procedures Performed.

	No. of Patients (%)
Maxillary antrostomy	53 (59.6)
Partial ethmoidectomy	53 (59.6)
Total ethmoidectomy	44 (49.4)
Sphenoidotomy	31 (34.8)
Frontal sinusotomy	29 (32.6)
Septoplasty	36 (40.5)
Radiofrequency ablation for inferior turbinates volume reduction	52 (58.4)
Immunotherapy	60 (67.4)

of chronic sinonasal diseases and any olfactory impairment were recruited as controls.

Diagnosis was based on history, clinical examination, nasal endoscopy, sinus-computed tomography scanning, skin prick testing (SPT) for atopy, test of pulmonary function, and olfactory testing. None of the subjects used oral or nasal corticosteroids and antibiotics 4 weeks prior to inclusion and oral antihistamines 1 week prior to SPT. All patients fulfilled the criteria of CRS and AR according to the EPOS²¹ and ARIA⁴ guidelines. All subjects underwent a brief psychiatric interview to exclude those with preexisting major psychiatric disorder.

ESS was the treatment of choice for CRS patients after failing broad-spectrum or culture-directed antibiotics in addition to a trial of oral and topical steroid therapy. It was conducted by a single surgeon following Messerklinger²² technique, according to the extent of the disease, with the use of microdebrider device. Septoplasty was implemented whenever significant septal deviation was present. Inferior nasal turbinates (INT) volume reduction was carried out by submucosal radiofrequency tissue ablation when INT enlargement was observed. Postoperative care included multiple visits at the outpatient clinic, where nasal endoscopy and toilette as needed were performed. All patients were asked to rinse their noses with sodium chloride solution and nasal steroids. AR patients were treated by immunotherapy for the specific aeroallergens that were sensitized for a consecutive period that ranged from 2 to 5 years. The frequencies of treatment protocols performed are reported in Table I. The study protocol was approved by the local Institutional Review Board. All subjects signed informed consent. The study was performed in accordance with the Declaration of Helsinki/Hong Kong.

Olfactory function of all patients and controls was assessed using Sniffin' Sticks test package (Burghart, Wedel, Germany) pre- and 12 months after treatment. At these time points, subjects also filled in six widely used questionnaires either specific for olfaction-associated QoL (Questionnaire of Olfactory Deficits-QOD) and for assessing mental health (Beck Depression Inventory-BDI, Zung Depression Scale-ZDS, Zung Anxiety Scale-ZAS, State and Trait Anxiety Inventory-STAI), or a general health survey (Short Form-SF-36).

Sniffin' Sticks test battery included specific tests for odor threshold (OT), odor discrimination (OD), and odor identification (OI).²³ Results of each one of the three tests were combined to a TDI score.²³ TDI score ranges from 0 to 48 (values of 15 or less represent anosmia; values between 16 and 34.5 represent hyposmia; and values over 34.5 represent normosmia for the mild climate conditions in Greece).²⁴

QOD is a validated olfaction-specific questionnaire for QoL.²⁵ It consists of 25 4-scale statements (17 negative, 2 positive, 6 socially desired) with a maximum score of 57 points.²⁵ High scores indicate a strong impairment in QoL.

SF-36 represents a widely used general-health related survey that assesses QoL in eight domains covering both physical and mental health from the patient's point of view with chronic diseases.^{26,27} Scores range from 0 to 100, with a higher score representing better functioning.^{26,27}

The other four questionnaires were used to assess QoL of patients detecting specifically their psychological profile. Depressive symptoms were assessed using the Greek-validated versions of BDI²⁸ and ZDS.²⁹ BDI consists of 21 self-reporting items graded from 0 to 3, and a higher score indicates higher level of depression. ZDS is another self-administered instrument measuring depression.²⁹ It consists of 20 items graded from 1 to 4 and assesses psychological and somatic depression. Higher scores indicate higher level of depression. Anxiety was assessed with ZAS³⁰ and STAI³¹ scales translated and validated in Greek. ZAS is a self-rating scale with a structure similar to ZDS.³⁰ STAI is an instrument consisting of two parts, one that refers to anxiety due to a specific condition (state), and one that refers to the general tendency of the subject to react anxiously (trait).³¹ Each one of these parts has 20 questions, which are answered by choosing between grades 1 to 4.

Data statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 19.0. The normality of quantitative variables was ascertained with Kolmogorov-Smirnov test. The scores of all questionnaires were expressed as the mean and standard deviation (SD). Differences in the scores of the questionnaires for QoL were assessed by Student's *t* test (for independent or paired samples) and one-way analysis of variance (ANOVA); post hoc analysis was performed using Tukey's test. Pearson's *r* correlation coefficient was used to assess the relation of TDI changes with the changes of the QoL questionnaires scores. Since the distribution of BDI score was skewed, the statistical analysis was performed on the log-transformed scores. Quantitative variables were expressed as frequencies and percentages (%) and they were analyzed using the chi-square test. For the evaluation of the significance of TDI changes, for the discrimination between clinically significant improvement or not of each QoL questionnaire separated, the area under the receiver operating characteristic (ROC) curve (AUC) was calculated. Sensitivity and specificity were also calculated. The value with the shortest distance from the curve to the point with both maximum sensitivity and specificity—that is, the point (0.0, 1.0)—was selected as the cutoff score to classify patients with clinically significant improvement on QoL. Multivariate logistic regression analysis was used to explore the independence of effects of olfactory improvement on QoL scale results, adjusted for all patients' demographics and clinical characteristics. All tests were two-tailed and statistical significance was considered for *P* values of less than 0.05.

RESULTS

Eighty-nine patients [53 suffering from chronic rhinosinusitis and 36 from allergic rhinitis; 51 (57.3%) males, mean age: 39.83 ± 16.05 years] and 30 healthy subjects [16 (53.3%) males, mean age: 37.03 ± 13.09 years] participated. Demographics and disease characteristics of all patients and controls are summarized in Table II. Regarding to the quantitative assessment of subjects' olfactory function with the use of Sniffin' Sticks test, patients presented statistically significant lower

TABLE II.
Demographics and Disease Characteristics of Patients and Healthy Controls Pretreatment.

	Control Group (n = 30)	Patients (n = 89)	P Value
Male gender [no (%)]	16 (53.3)	51 (57.3)	0.705
Age [years; mean (SD)]	37.03 (13.09)	39.83 (16.05)	0.389
Socioeconomic status [no (%)]			0.140
Low	1 (3.3)	8 (9.0)	
Medium	14 (46.7)	25 (28.1)	
High	15 (50.0)	56 (62.9)	
Smoking [no (%)]	9 (30.0)	31 (34.8)	0.628
Duration of smoking [years; median (IQR)]	7 (15–25)	11 (9–30)	0.215
Disease characteristics [no (%)]			
Allergic Rhinitis [no (%)]	–	60 (67.4)	
Chronic rhinosinusitis [no (%)]	–	53 (59.5)	
Nassal polyps [no (%)]	–	25 (28.1)	
Asthma presence [no (%)]		13 (14.6)	
TDI score [mean (SD)]	38.93 (1.42)	27.92 (12.22)	<0.001
Olfactory function [no (%)]			
Normosmics	30 (100.0)	40 (44.9)	
Hyposmics	–	30 (33.7)	
Anosmics	–	19 (21.3)	
Duration of olfactory dysfunction [years]	–	5 (3–12)	

TDI score compared to controls [27.92 ± 12.22 (range, 2–39.25) versus 38.93 ± 1.42 (range, 37–40), $P < 0.001$]. Based on this score, 49 (55.1%) patients presented olfactory dysfunction; 19 (21.4%) were anosmics; and 30 (33.7%) were hyposmics. The duration of olfactory deficit ranged from 1 to 30 years, with a median duration of 5 years (interquartile range, 3–12 years). All the subjects of the control group were normosmics. Among patients, higher frequency of anosmia was associated with female gender (34.2% vs. 11.8%, $P = 0.011$), ages older than 55 years (60.9% vs. 7.6%, $P < 0.001$), lower socioeconomic status (62.5% vs. 24.0% and 14.3% in medium and high social status, $P = 0.007$), chronic rhinosinusitis (32.1% vs. 5.6% in allergic rhinitis, $P = 0.003$) and asthma (69.2% vs. 13.2%, $P < 0.001$).

The scores of olfactory function and QoL questionnaires of patients and controls are shown in Table III. Patients exhibited statistically significant worse pretreatment scores in all questionnaires (all $P < 0.05$) compared to healthy controls. Throughout the 12-month follow-up time, all indices of olfactory function exhibited highly significant elevation: odor threshold (OT) by 48.6% ($P < 0.001$), odor discrimination (OD) by 21.7% ($P < 0.001$), odor identification (OI) by 23.8% ($P < 0.001$), and TDI score by 27.4% ($P < 0.001$). In particular, TDI score was improved in the majority of the patients (79 patients, 88.8%) by 0.75 to 31.5 points; and it remained unchanged in seven (7.9%) and was reduced only in three (3.3%) patients (by 6.5, 5, and 2 points). Nevertheless, posttreatment scores of olfactory function, in total

and in separate CRS groups, remained significantly (all $P < 0.05$) lower compared to healthy controls. Furthermore, we observed that treatment was ensued by a significant improvement in the scores of all QoL questionnaires, too. The greatest improvement was observed in QOD scores (by -44.7% , $P < 0.001$) and its subscales QOD-NS (-86.5% , $P < 0.001$) and QOD-SD (-52.4% , $P < 0.001$). Lower, but statistically significant improvement was observed in the overall SF-36 score (by 20.7% , $P < 0.001$) in all of its dimensions (6.5%–35.3%, all $P < 0.010$) and in all psychological scales (ZAS: -20.6% , $P < 0.001$; STAI: -18.1% , $P < 0.001$; ZDS: -17.4% , $P < 0.001$; BDI: -32.5% , $P < 0.001$) (Table III). Moreover, analyzing the CRS and AR groups of patients separately, statistically significant changes of the olfactory function and all psychometric QoL questionnaires results were also found in patients with AR (TDI: 10.4% , $P = 0.004$; QOD: -32.3% , $P = 0.009$; SF-36: 15.1% , $P < 0.001$; ZAS: -13.8% , $P < 0.001$; STAI: -15.8% , $P < 0.001$; ZDS: -12.3% , $P < 0.001$; BDI: -37.5% , $P = 0.036$) as well as in patients with CRS (TDI: 39.9% , $P < 0.001$; QOD: -49.8% , $P < 0.001$; SF-36: 25.1% , $P < 0.001$; ZAS: -24.2% , $P < 0.001$; STAI: -19.5% , $P < 0.001$; ZDS: -20.4% , $P < 0.001$; BDI: -31.0% , $P < 0.001$). Posttreatment scores of all questionnaires reached the scores of the control group in total and in separate CRS and AR groups of patients as well, with the exception of QOD [total cohort: 7.79 (3.50) versus 6.27 (0.78), $P = 0.001$; CRS: 8.45 (4.32) versus 6.27 (0.78), $P < 0.001$] and its subscales, which remained significantly worse compared to healthy controls.

The rehabilitation of olfaction was significantly associated with the improvement of patients' QoL and MH, as it was disclosed by the correlation analysis between the 12 month-changes of TDI ($\Delta\text{TDI}_{0,12}$) and the following psychometric questionnaires (in descending order of the size of correlation coefficient): QOD ($r = -0.738$, $P < 0.001$), ZAS ($r = -0.361$, $P = 0.001$), STAI ($r = -0.359$, $P = 0.001$), BDI ($r = -0.347$, $P = 0.001$), ZDS ($r = -0.284$, $P = 0.007$) and SF-36 ($r = 0.316$, $P = 0.003$) (Table IV). Similar correlations were found when the analysis was stratified according to the type of the disease (Table IV).

Clinically significant improvement was defined for each QoL questionnaire as a change of $\geq 1/2$ SD of the pretreatment score³² and it was obtained by 39 (43.8%) patients for BDI to 60 (67.4%) patients for ZAS and STAI scales (in details; see Table V). ROC analysis was used for the discrimination between clinically significant improvement or not of each QoL questionnaire separated, based on the changes of the TDI score. The area under the ROC curve (AUC) was ranging from 0.604 to 0.862. The same optimal cutoff score of 4.25 points improvement of the TDI was determined for all questionnaires; and it remained independently associated with clinically significant improvement in multivariate logistic regression analysis, adjusted for all patients' characteristics. When considering only hyposmic and anosmic patients, the results described above remained the same with the entire cohort. This cutoff score yielded sensitivities ranging from 54.3% to 77.5% and

TABLE III.
Scores of Olfactory Function and Quality of Life (QoL) Questionnaires Pre- and 12 Months After Treatment.

	Olfactory and Psychometric Scores				% Change	P Value
	Control Group	Patients				
		Pretreatment	Posttreatment			
<i>Olfactory scores</i>						
O.T.	8.13 (0.71)	5.00 (2.35)*	7.43 (5.38)*	48.6	<0.001	
O.D.	15.60 (0.62)	11.82 (4.86)*	14.39 (2.63)*	21.7	<0.001	
O.I.	15.20 (0.55)	11.10 (5.10)*	13.74 (2.63)*	23.8	<0.001	
T.D.I.	38.93 (1.42)	27.92 (12.22)*	35.56 (6.64)*	27.4	<0.001	
<i>QoL questionnaires</i>						
QOD	6.27 (0.78)	14.09 (7.70)*	7.79 (3.50)*	−44.7	<0.001	
QOD-NS	0.00 (0.00)	6.80 (5.82)*	0.92 (6.62)*	−86.5	<0.001	
QOD-PS	6.00 (0.00)	4.75 (1.24)*	5.65 (0.87)*	18.9	<0.001	
QOD-SD	0.27 (0.20)	2.54 (1.65)*	1.21 (0.90)*	−52.4	<0.001	
SF-36 (total)	86.86 (10.10)	72.93 (15.72)*	88.00 (9.00)	20.7	<0.001	
GH (general health)	71.86 (18.93)	60.07 (19.43)*	79.06 (13.58)	31.6	<0.001	
PF (physical functioning)	93.33 (8.02)	80.00 (19.42)*	90.56 (12.74)	13.2	<0.001	
RP (role physical)	93.33 (25.37)	69.66 (28.52)*	94.27 (14.37)	35.3	<0.001	
RE (role emotional)	95.56 (16.91)	74.53 (28.34)*	94.76 (14.13)	27.1	<0.001	
SF (social functioning)	89.58 (11.87)	83.57 (18.42)*	95.76 (8.23)	14.6	<0.001	
BP (body pain)	96.17 (6.46)	87.67 (16.94)*	93.37 (13.68)	6.5	0.002	
VT (vitality)	78.00 (15.18)	68.09 (21.88)*	83.76 (12.97)	23.0	<0.001	
MH (mental health)	84.20 (6.81)	68.40 (19.46)*	82.38 (12.44)	20.4	<0.001	
Zung Anxiety Scale	29.97 (6.16)	36.89 (9.82)*	29.28 (6.85)	−20.6	<0.001	
STAI	34.83 (8.40)	41.76 (9.82)*	34.21 (8.79)	−18.1	<0.001	
Zung Depression Scale	28.43 (5.57)	37.13 (8.68)*	30.66 (6.42)	−17.4	<0.001	
Beck Depression Inventory	5.07 (3.56)	9.55 (6.26)*	6.45 (5.16)	−32.5	<0.001	

Data are expressed as mean values.

*Statistically significant ($p < 0.05$) worse scores compared to control group; SD = standard deviation.

specificities ranging from 51.7% to 73.5%. In the sequence, ROC analysis was performed separately within the two groups of patients (AR: AUC ranged from 0.600 to 0.961; CRS: AUC ranged from 0.621 to 0.866); it revealed that the optimal cutoff scores of 3.50 and 4.75 points improvement of the TDI among patients with AR and CRS diseases, respectively, were associated with the clinically significant improvement of all questionnaires (AR: sensitivities ranged from 50.0% to 91.7% and specificities ranged from 57.1% to 83.3%; CRS: sensitivities ranged from 52.6% to 84.0% and specificities ranged from 53.3% to 82.1%). However, the changes of the TDI score in the 4th quartile (all patients: $\Delta\text{TDI}_{0,12} > 8.75$ points; AR: $\Delta\text{TDI}_{0,12} > 5.60$ points; CRS: $\Delta\text{TDI}_{0,12} > 10.50$ points) were associated with statistically significant (all $P < 0.05$) greater improvement of all QoL scales outcomes compared to the 1st, 2nd, and 3rd quartiles (Table VI).

DISCUSSION

This is the first study to provide objective data with respect to the improvement values of olfactory function, expressed in the TDI score perceived in patients' everyday lives and lead to QoL recovery outcomes. Approaching two common, chronic associated sinonasal

diseases,^{1-4,33} which consist of the vast majority of olfactory disorders etiology³ that nevertheless can be reversed, but influence patients' QoL and MH, we aimed to show the importance of olfactory function and its recovery on patients' QoL. These patients were the best candidates to study olfaction/QoL correlations during treatment with clinical importance.

We found that olfactory function recovers and this is expressed by a significant improvement in the TDI and all separate test (O.T, O.D, O.I) scores in total and in each group separately. Regarding olfactory recovery the percentage for AR patients was smaller than CRS patients (10.4% vs. 39.9%), although highly significant, due to the fact that olfactory status of AR patients at baseline was better than CRS ones. Olfactory rehabilitation was followed by patients' QoL and psychological state recovery as well; there was a significant improvement in the results of all questionnaires used for the assessment of patients' QoL and MH. Moreover, we observed that the TDI score was significantly correlated to all QoL scale results. The higher the improvement for olfaction, the higher was the score for QoL in all psychometric tests—and for both diseases as well. Therefore, we proved the outstanding impact of olfaction recovery on patients' QoL and MH in terms of TDI score results.

TABLE IV.
Association Between the Change of the Olfactory Function (ΔTDI_{0-12}) and the Changes of All Psychometric Questionnaires, Expressed as Pearson's r Correlation Coefficient.

Change of Psychometric Questionnaires	Change of the Olfactory Function (ΔTDI_{0-12})		
	Total	AR	CRS
$\Delta\text{QOD}_{0,12}$	-0.738 [‡]	-0.841 [‡]	-0.568 [‡]
$\Delta\text{QOD-NS}_{0,12}$	-0.755 [‡]	-0.839 [‡]	-0.604 [‡]
$\Delta\text{QOD-PS}_{0,12}$	0.061	-0.105	0.069
$\Delta\text{QOD-SD}_{0,12}$	-0.200	-0.150	-0.194
$\Delta\text{SF-36}_{0,12}$	0.316 [†]	0.483 [†]	0.293 [*]
$\Delta\text{GH}_{0,12}$ (general health)	0.045	0.173	0.196
$\Delta\text{PF}_{0,12}$ (physical functioning)	0.431 [‡]	0.458 [†]	0.291 [*]
$\Delta\text{RP}_{0,12}$ (role physical)	0.332 [‡]	0.500 [†]	0.287 [*]
$\Delta\text{RE}_{0,12}$ (role emotional)	0.273 [*]	0.170	0.140
$\Delta\text{SF}_{0,12}$ (social functioning)	0.237 [*]	0.227	0.192
$\Delta\text{BP}_{0,12}$ (bodily pain)	-0.164	-0.126	-0.185
$\Delta\text{VT}_{0,12}$ (vitality)	0.125	0.099	0.125
$\Delta\text{MH}_{0,12}$ (mental health)	0.203	0.046	0.199
$\Delta\text{Zung Anxiety Scale}_{0,12}$	-0.361 [‡]	-0.326 [*]	-0.334 [*]
$\Delta\text{State and Trait Anxiety Inventory}_{0,12}$	-0.359 [‡]	-0.339 [*]	-0.433 [*]
$\Delta\text{Zung Depression Scale}_{0,12}$	-0.284 [‡]	-0.343 [†]	-0.276 [†]
$\Delta\text{Beck Depression Inventory}_{0,12}$	-0.347 [‡]	-0.586 [‡]	-0.308 [*]

^{*} $p < 0.05$

[†] $p < 0.01$

[‡] $p < 0.001$

Prior studies have already reported the positive effects of ESS and immunotherapy for patients' QoL either in CRS⁷⁻¹⁵ or AR¹⁶⁻²⁰ diseases. However, these studies focused mainly on the effects of symptoms resolution on patients' QoL, without providing clinically important information for olfaction/QoL correlations. To the best of our knowledge, this is the first study to address the direct positive relationship of olfactory recovery rates with QoL and psychological outcomes, using olfaction-and mental health-specific questionnaires—as well as quantitative smell tests for the assessment of olfactory performance—thus providing objective data for olfactory function and not self-reporting symptoms for these common diseases. It is clinically important to mention that according to all questionnaire results (with the exception of QoL in total and CRS groups), patients' QoL and psychological state are fully restored, and reach the outcomes of healthy subjects 12 months after treatment, either in CRS or AR diseases. QoD as specific for reflecting olfaction-associated QoL follows changes on TDI score that remains in CRS patients significantly worse compared to healthy controls.

Additionally, this study for the first time quantitatively explores the improvement values of olfactory function expressed in the TDI score, which results in a clinically significant improvement of QoL and MH as well. In a recent study, Gudziol et al.³⁴ related the self-

assigned changes of olfactory function in patients with smell disorders with results from olfactory testing by means of Sniffin' Sticks test. They found that an increase in olfactory sensitivity by 5.5 points in the TDI score is perceived as such from patients. In our study an olfactory recovery by 4.25 points, in total cohort, proved to be the cutoff limit for a clinically significant improvement in all QoL scales, with values of all questionnaires to start approaching the results of healthy subjects. Similar cutoff points were detected after the two groups of patients were analyzed separately (3.50 points for AR and 4.75 points for CRS patients). However, this improvement further continued, and when the changes of the TDI score became even higher (8.75 points in total, 5.60 for AR and 10.50 for CRS groups), patients' QoL and psychological state were totally restored. Our results provide important data for olfaction/QoL correlations for populations living in mild climate conditions that are known to influence olfaction,²⁴ and the effects on patients' daily lives are based on specific questionnaires for QoL assessment results and not self-assigned records that may be misleading.^{35,36} These findings might be the basis for better counselling our patients suffering from CRS and AR with regard to the results of a specific therapy for olfactory deficit due to a possible gain in QoL.

CONCLUSION

Quality of life and mental health of patients suffering from chronic sinonasal diseases such as CRS and AR are fully recovered after treatment, getting the results of healthy subjects; the latter's recovery goes in parallel with smell improvement. An increase by 3.50 points for AR and 4.75 points for CRS patients for olfactory function, expressed by the TDI score, is ensued by a statistically significant improvement in all QoL questionnaires, and has been proved for the first time to be the cutoff points for their outcomes to be clinically significant recovered. QoL instruments proved to be useful tools for doctors in everyday clinical practice during consultation for treatment, for selection of appropriate patients, and for therapy control that may further improve outcomes and patients' QoL.

TABLE V.
Cut-Off Limits for Clinically Significant Improvement on Each QoL Questionnaire and No. of Patients (%) That Achieved Such a Clinically Significant Improvement.

	All Patients		AR		CRS	
	Cutoff	No. (%)	Cutoff	No. (%)	Cutoff	No. (%)
QOD	≤ -3.85	40 (44.9)	≤ -3.84	12 (33.3)	≤ -5.01	25 (47.2)
SF-36	≥ 7.86	56 (62.9)	≥ 6.60	29 (80.6)	≥ 7.84	34 (64.2)
ZAS	≤ -4.91	60 (67.4)	≤ -2.86	26 (72.2)	≤ -5.18	41 (77.4)
STAI	≤ -4.91	60 (67.4)	≤ -4.20	22 (61.1)	≤ -5.00	38 (71.7)
ZDS	≤ -4.34	46 (51.7)	≤ -3.07	22 (61.1)	≤ -4.71	31 (58.5)
BDI	≤ -3.13	39 (43.8)	≤ -2.46	14 (38.9)	≤ -4.48	14 (26.4)

AR = allergic rhinitis; CRS = chronic rhinosinusitis.

TABLE VI.
Changes of Psychometric Questionnaires in Relation to the Changes of the Olfactory Function (expressed by TDI score).

All Patients	Changes in TDI Score			
	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
QOD	-0.70 (1.83)	-6.29 (8.83)	-6.64 (5.45)	-14.82 (11.66)
SF-36	7.98 (5.50)	9.20 (8.20)	15.05 (10.94)	23.23 (15.74)
Zung Anxiety Scale	-6.90 (4.82)	-6.86 (4.29)	-6.45 (4.52)	-12.14 (8.57)
State and Trait Anxiety Inventory	-6.80 (4.37)	-5.81 (5.28)	-7.71 (5.65)	-12.06 (9.32)
Zung Depression Scale	-4.93 (5.73)	-7.30 (4.22)	-6.18 (5.11)	-9.55 (6.69)
Beck Depression Inventory	-2.29 (1.49)	-3.10 (2.56)	-4.05 (4.58)	-5.55 (6.04)
AR				
QOD	-0.22 (0.41)	0.29 (2.62)	-3.22 (6.18)	-8.00 (9.99)
SF-36	8.08 (4.60)	9.27 (3.48)	12.64 (7.90)	17.27 (13.85)
Zung Anxiety Scale	-1.89 (3.40)	-3.28 (6.31)	-5.11 (2.66)	-6.45 (4.08)
State and Trait Anxiety Inventory	1.55 (5.56)	-6.00 (4.69)	-8.28 (4.31)	-11.40 (5.54)
Zung Depression Scale	-1.11 (3.48)	-3.11 (2.47)	-5.22 (2.99)	-7.31 (4.98)
Beck Depression Inventory	1.33 (4.16)	-3.28 (3.04)	-2.89 (3.02)	-5.00 (5.55)
CRS				
QOD	-0.15 (1.95)	-8.00 (7.36)	-10.00 (5.25)	-15.85 (12.77)
SF-36	10.35 (9.64)	14.87 (9.98)	15.01 (12.71)	32.35 (12.63)
Zung Anxiety Scale	-6.69 (5.52)	-7.41 (5.43)	-11.10 (7.44)	-14.95 (9.27)
State and Trait Anxiety Inventory	-7.77 (3.21)	-6.88 (5.31)	-8.25 (5.20)	-12.73 (12.61)
Zung Depression Scale	-5.15 (3.84)	-7.71 (6.21)	-8.15 (6.47)	-11.30 (6.68)
Beck Depression Inventory	-1.85 (1.52)	-3.71 (3.28)	-3.70 (3.56)	-6.08 (6.56)

Data are expressed as mean change.

AR = allergic rhinitis; CRS = chronic rhinosinusitis; SD = standard deviation.

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