Association between olfactory function and quality of life in patients with olfactory disorders: a multicenter study in over 760 participants*

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Abstract

Background: This cross-sectional, multi-centric study aimed to investigate the differences in quality of life among patients with olfactory dysfunction (OD) of different origin, and to identify factors associated with olfactory-related quality of life (QOL).

Methods: Seven hundred sixty-three adults were recruited from 8 Smell & Taste clinics in Germany, Switzerland, and Austria. Olfactory-related QOL was assessed by the Questionnaire of Olfactory Disorders (QOD). Olfactory function was assessed with the "Sniffin' Sticks" test; self-assessment was performed with visual analog scales.

Results: Patients with post-infectious and post-traumatic OD showed poorer olfactory-related QOL than patients with sinonasal and idiopathic OD. The olfactory-related QOL was positively associated with the Sniffin' Sticks test score, self-assessed olfactory function, disease duration, and age, with younger olfactory dysfunction patients showing lower QOL. Female patients presented with poorer olfactory-related QOL. In addition, the results showed that self-assessment of olfactory function explained more of the variance in olfactory-related QOL than olfactory function evaluated by the Sniffin' Sticks test.

Conclusions: In addition to the psychophysical testing results, several factors such as disease cause, disease duration, sex, or self-assessed olfactory dysfunction should be taken into account when assessing the individual severity of the smell loss.

Key words: anosmia, hyposmia, olfactory disorder, parosmia, quality of life, smell loss

Introduction

Olfactory dysfunction (OD) is a common problem, which occurs in 13-24% of the general population [1-6]. OD may have a significant impact on quality of life (QOL), as olfaction plays a vital role in many important areas, like food enjoyment, cooking, avoidance of danger, and to some extent in social situations and working life [7,8]. Previous studies provided evidence that general QOL is reduced in patients with OD [9-12].

The Questionnaire of Olfactory Disorders (QOD) developed by Frasnelli and Hummel [13], has been widely used to specifically assess olfactory-related QOL. To date, the QOD has been proven to be a generally reliable and valid questionnaire for use also in several other countries [14-17].

Olfactory dysfunction has many etiologies, the most common causes of olfactory dysfunction are sinonasal, postinfectious, posttraumatic and idiopathic [18]. A few studies have demonstrated poorer olfactory-related QOL and its relationship with olfactory function in patients with chronic rhinosinusitis and allergic rhinitis [19,20], post-traumatic brain injury [21], and in other patients [14,15,17]. However, very little is currently known about olfactory-related QOL in patients with very common causes of OD, like postinfectious, and idiopathic. In addition, there is no comparative knowledge about differences of olfactory-related QOL among OD patients with different causes. Even if the measurable olfactory impairment seems to be similar, the QOL appears to differ between patient groups.

Most previous studies of olfactory-related QOL in OD recruited patients from a single clinic, which may bias the results because of the sample size being small, or only comprising of patients with limited causes of the disease. To overcome the possible bias, we performed a multicenter study to assess the impact of OD on olfactory-related QOL in a large sample of patients from 8 clinics in Germany, Switzerland and Austria. The aim of this study was to investigate the differences among OD patients with different causes, and to identify factors associated with olfactory-related QOL in a large cohort of OD patients.

Methods

Participants

In this cross-sectional study, 777 adult patients with subjective complaints of olfactory disorder were recruited from 8 Smell & Taste clinics in Dresden (TUD, Dresden, Germany; n=319), Heidelberg (Universitätsklinikum Heidelberg, Germany; n=48), Jena (Universitätsklinikum Jena, Germany; n=102), Berlin (HNO Zentrum am Kudamm, Berlin, Germany; n=44), Cologne (Universitätsklinikum Köln, Cologne, Germany; n=110), Basel (Universitätsspital Basel, Switzerland; n=55), Bern (Inselspital Bern, Switzerland; n=37), and Vienna (Medizinische Universität Wien, Vienna, Austria; n=62), respectively. All patients were thoroughly diagnosed according to the current diagnostic ORL criteria for smell disorders [18] including anterior rhinoscopy, nasal endoscopy, olfactory testing, and MR imaging which ensures correct diagnosis assignment. The diagnosis of a sinunasal olfactory disorder was based on the presence of inflammatory diseases of the nose or the paranasal sinuses such as chronic rhinosinusitis with or without nasal polyposis. In patients with the diagnosis of a post-infectious olfactory dysfunction, the loss of smell has existed since an upper respiratory tract infection and is characterized by a sudden onset. The diagnosis post-traumatic olfactory disorder related to an olfactory impairment following a head injury. In contrast, in the case of an idiopathic olfactory disorder, no cause of the olfactory disturbance could be determined. Neurodegenerative smell loss was diagnosed in those patients whose olfactory dysfunction was secondary to Parkinson´s disease. For the diagnosis of congenital smell loss, severe olfactory impairment from birth and hypoplastic/aplastic olfactory bulbs and olfactory sulci were required.

In addition, we recruited 30 healthy controls without olfactory disorders and any underlying disease. The study was approved by the Ethics committee at each institution and all the participants provided written informed consent.

Measures

Sociodemographic data, including age and sex, as well as information on disease cause and duration were collected.

The Sniffin' Sticks test, comprising olfactory threshold (T), discrimination (D) and identification (I) tests, was used to evaluate olfactory function.22 The maximum score for each test was 16. The sum of the three tests was presented as a total TDI score (range 1-48). The TDI score was used to define functional anosmia (TDI ≤ 16), hyposmia (16 < TDI < 31), or normosmia (TDI ≥ 31). If the participant had only finished the identification test, the I score was used to define functional anosmia (I ≤ 8), hyposmia (8 < I ≤ 11), or normosmia (I > 11). Examinations were performed bilaterally testing both nostrils simultaneously.

The QOD comprises two parts: 1) 29 items with 3 subscales: 19 items on quality of life (QOD-QOL); 6 items on social desirability (QOD-DS); 4 items on parosmia (QOD-P); and 2) 5 visual analog scales (QOD-VAS) concerning problems related to olfactory dysfunction at work, in family and social life. In the first part, participants could agree, partly agree, partly disagree, disagree for each item. According to the item and the response, the participant's answer was scored from 0 to 3 points. The sum of the scores for QOD-QOL and QOD-P ranged 0-57 and 0-12, respectively. A higher score indicates a worse impairment. The sum of QOD-DS scores ranged 0-18. A higher score means a tendency toward giving a socially desired answer which means the results are less credible. The QOD-VAS total scored from 0 to 50 points based on the results of 5 single VAS scales with its left-hand end defined as "not at all" (0 units), and the right–hand end defined as highest frequency possible ("always"- 10 units). A higher QOD-VAS score indicates a worse impairment.

Self-assessed olfactory function was rated on an 8-point scale scoring from 0 (no olfactory perception at all) to 7 (very good smell) modified according to the Smell & Taste history questionnaire used in German speaking countries [23].

Statistical analysis

All statistical analyses were performed using the IBM SPSS 23.0 (IBM Corp., Armonk, NY, USA). All statistical tests were 2 sided,

Table 1. Single center cases of brainstem lesions approached via an extended endoscopic endonasal approach.

Diagnosis	N	Female N (%)	Age (years) (mean ± SD)	Duration (years) (mean ± SD)	Anosmia N (%)	Hypos-mia N (%)	Nor-mosmia N (%)	QOD-P (mean ± SD)	QOD-QOL (mean ± SD)	QOD-VAS (mean ± SD)	QOD-DS (mean ± SD)
Controls	30	17 (56.7)	51.13 ±15.65	/	/	/	/	1.47 ±1.91	8.10 ±6.68	/	11.63 ±3.22
Patients	733	309 (42.2)	56.28 ±14.39	3.51 ±6.57	365 (49.8)	311 (42.4)	57 (7.8)	3.65 ±3.01	20.12 ±11.09	27.52 ±12.34	12.33 ±3.05
Sinonasal	122	63 (51.6)	52.71 ±14.78	5.21 ±7.44	68 (55.7)	40 (32.8)	14 (11.5)	3.26 ±3.00	18.84 ±11.53	25.95 ±13.78	12.12 ±2.94
Post-infectious	243	70 (28.9)	57.64 ±11.75	1.67 ±4.23	88 (36.2)	138 (56.8)	17 (7.0)	4.37 ±3.13	22.53 ±10.55	30.83 ±10.99	12.44 ±3.26
Post-traumatic	108	49 (45.4)	50.68 ±16.24	3.10 ±5.87	77 (71.3)	27 (25.0)	4 (3.7)	4.16 ±3.09	24.32 ±11.97	29.23 ±11.69	11.69 ±2.78
Idiopathic	242	119 (49.2)	60.00 ±13.49	3.58 ±4.82	119 (49.2)	104 (43.0)	19 (7.9)	3.02 ±2.71	17.11 ±9.96	23.96 ±11.99	12.66 ±3.03
Neuro degenerative	7	2 (28.6)	64.09 ±17.75	2.49 ±1.33	2 (28.6)	2 (28.6)	3 (42.9)	3.14 ±2.04	13.86 ±10.25	25.35 ±11.73	12.00 ±2.94
Congenital	11	6 (54.5)	34.00 ±18.00	27.55 ±18.19	11 (100)	0(0)	0(0)	1.27 ±1.27	14.36 ±7.41	18.12 ±12.73	11.27 ±1.49
F	/	/	15.51**	46.07**	/	/	/	7.68**	11.33**	8.35**	1.97

QOD-P: Questionnaire of Olfactory Disorders-parosmia; QOD-QOL: Questionnaire of Olfactory Disorders-quality of life; QOD-DS: Questionnaire of Olfactory Disorders-socially desired; QOD-VAS: Questionnaire of Olfactory Disorders-visual analog scales; * P<0.05, **P<0.01

and $\alpha = 0.05$ was considered statistically significant. Multivariate analysis of variance (MANOVA) followed Bonferroni post-hoc tests were used to examine the differences in the QOD subscale scores in patients with different causes and healthy controls. The Pearson's coefficients of correlation between the QOD subscale scores and olfactory test scores were calculated.

A series of hierarchical regression analyses were performed to identify the potential factors influencing the QOD-QOL, QOD-P, and QOD-VAS separately, which included the variables age, sex, disease duration, disease causes, objective and subjective olfactory function (i.e., TDI scores and self-assessed olfactory function). Before entering variables into the analysis, dummy variables were constructed for the categorical variables (disease causes and sex). Age, sex and disease duration variables were entered in the regression model at the first step (Model 1), disease cause at the second step (Model 2), the TDI score at the third step (Model 3), and the self-assessed olfactory function at the fourth step (Model 4) to determine whether they explained a significant percentage of the variance in the outcome variables, i.e., QOD-QOL, QOD-P, and QOD-VAS separately.

Results

Demographics

Eight hundred and seven adults who were invited to attend in the study agreed to participate. Complete surveys were available for 763 adults (733 patients and 30 healthy controls), who made up the study sample. The etiology of olfactory disorder was idiopathic (242 patients), post-viral (243 patients), sinonasal (122 patients), post-traumatic (108 patients), neurodegenerative (7 patients) and congenital (11 patients). The patient demographic information, disease causes, and duration are given in Table 1.

Among the 733 patients, in 84 patients only the olfactory identification test was used, while all others finished the whole Sniffin' Sticks test. The mean threshold score of the Sniffin' Sticks test was 2.77±2.54, the mean discrimination score was 7.79±3.33, and the mean identification score was 7.32±3.68. The mean TDI score was 17.80±7.92. Based on the TDI score or identification score, 356 patients (48.57%) were considered as functionally anosmic, 327 patients (44.61%) were considered as hyposmic and 50 patients (6.82%) were considered as normosmic, despite the presence of complaints of olfactory dysfunction.

Differences in QOD scores among patients with different causes

The sample size of OD patients with neurodegenerative (7 patients) and congenital (11 patients) was small, so we just compared the differences in QOD scores among patients with idiopathic, post-viral, sinonasal and post-traumatic OD and healthy controls. The MANOVA results showed that QOD-QOL, QOD-P and QOD-DS differed significantly among the groups (all $p < 0.05$) (Table 1). Bonferroni post hoc testing revealed significant

Table 2. Correlations between variables.

	Duration	T	D	I	TDI	SA	QOD-P	QOD-QOL	QOD-VAS
Age (years)	-0.04	-0.14**	-0.03	-0.10**	-0.09*	0.08*	-0.01	-0.09*	0.02
Duration (years)		-0.07	-0.11**	-0.16**	-0.14**	-0.08*	-0.19**	-0.12**	-0.10*
T			0.44**	0.49**	0.73**	0.37**	0.07	-0.10*	-0.04
D				0.63**	0.85**	0.37**	0.12**	-0.12**	-0.08
I					0.88**	0.35**	0.11**	-0.09*	-0.05
TDI						0.43**	0.12**	-0.11**	-0.05
SA							-0.04	-0.28**	-0.34**
QOD-P								0.33**	0.28**
QOD-QOL									0.68**

T: olfactory threshold; D: olfactory discrimination; I: olfactory identification; TDI: total score of the olfactory threshold, discrimination and identification tests; SA: self-assessment olfactory function; QOD-P: Questionnaire of Olfactory Disorders-parosmia; QOD-QOL: Questionnaire of Olfactory Disorders-quality of life; QOD-VAS: Questionnaire of Olfactory Disorders-visual analog scales; * P<0.05; **P<0.01.

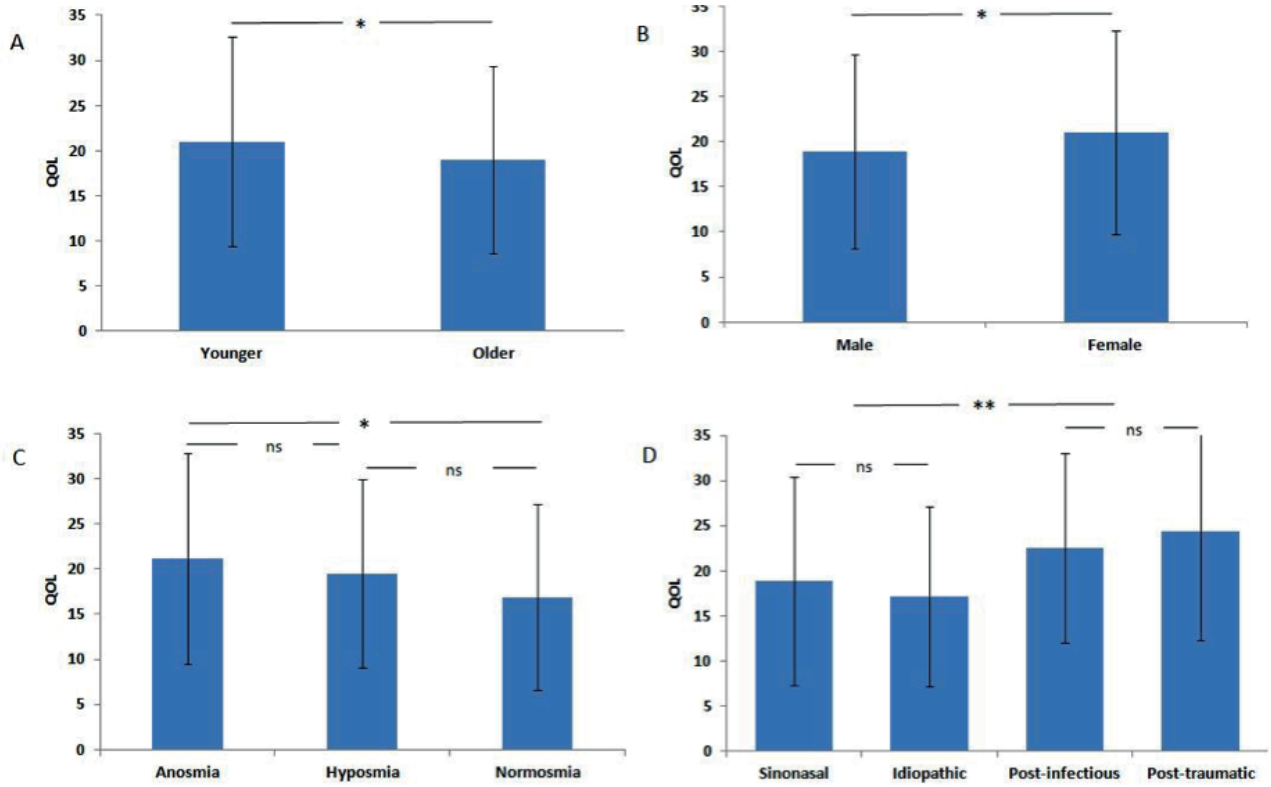

Figure 1. Differences on QOL among patients with different age, sex, olfactory function, and causes. Graph A indicated younger patients had higher scores in QOD-QOL than older patients (p<0.05). Graph B indicated male patients scored lower than female patients (p<0.05). Graph C showed significant difference was found between patients with anosmia and normosmia (p<0.05), and no significant difference was found between patients with hyposmia and anosmia or normosmia. Graph D showed the QOD-QOL scores in the sinonasal and idiopathic OD groups were lower than that in post-infectious and posttraumatic OD groups (all p < 0.01). Notes: QOL: quality of life; ns: non-significant; * p<0.05; ** p<0.01.

higher QOD-QOL score in each patient group than healthy controls (all p < 0.001). The QOD-QOL scores in the sinonasal and idiopathic OD groups were lower than that in post-infectious and posttraumatic OD groups (all p < 0.001) (Figure 1A). Bonferroni post hoc testing revealed that QOD-P in the sinonasal, post-infectious and posttraumatic patient groups was also higher than in healthy controls (all p < 0.001), but there was no difference between the idiopathic group and healthy group (p > 0.05). The QOD-P in the sinonasal and idiopathic OD groups was lower than in post-infectious and posttraumatic OD groups (all

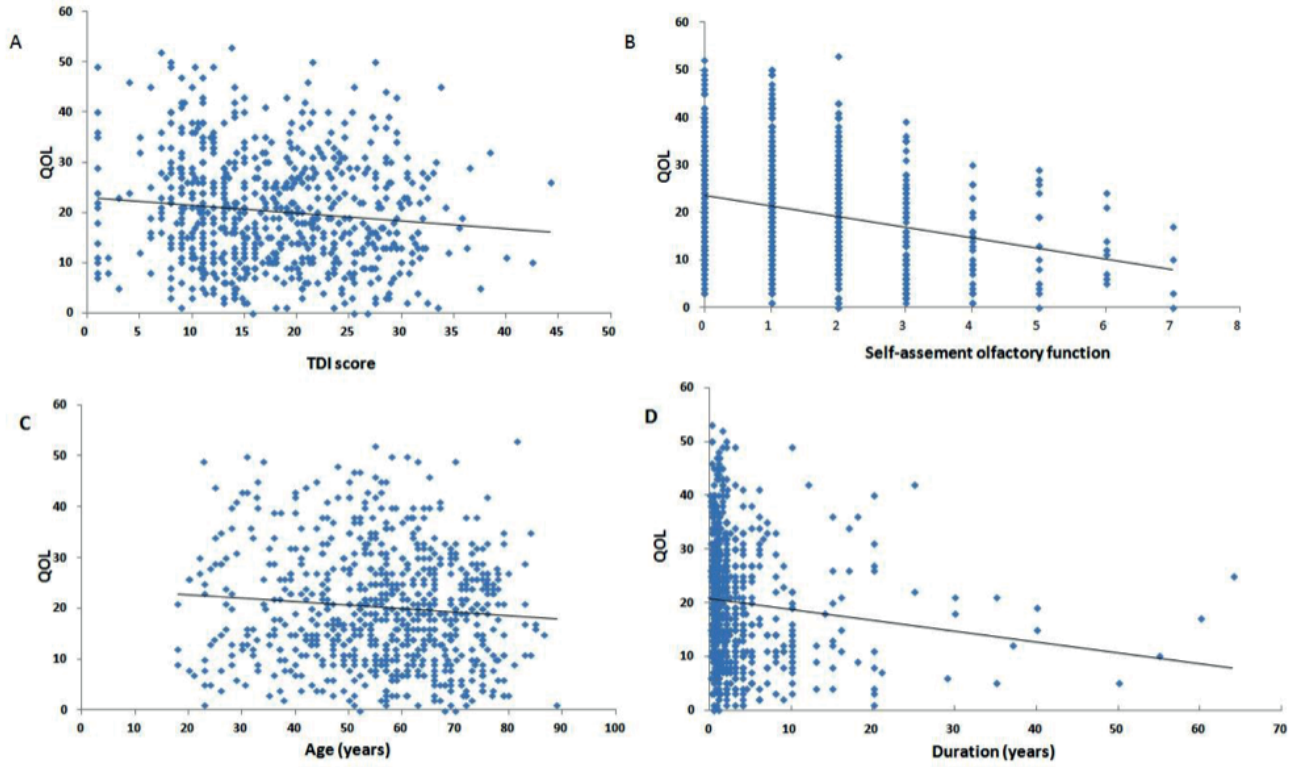

Figure 2. Relationship between QOL and tested and self-assessed olfactory function, age, and duration of smell loss. Graph A indicated TDI score was negatively associated with QOD-QOL score (r = -0.11, p <0.01). Graph B showed a negative correlation between self-assessed olfactory function and QOD-QOL score (r = -0.28, p <0.01). Graph C indicated older people showed lower score in QOD-QOL (r = -0.09, p <0.05). Graph D showed patients with longer disease duration had worse performance in QOD-QOL (r = -0.12, p <0.01). Notes: QOL: quality of life; TDI: total score of Sniffin' Sticks Test.

$p < 0.05$). In addition, there was no difference in QOD-DS among the groups (all $p > 0.05$).

The healthy controls were not assessed using the QOD-VAS, so we just compared the QOD-VAS among the patient groups. Complete data regarding QOD-VAS scores were available for 442 patients. The QOD-VAS in the sinonasal and idiopathic OD groups was lower than in post-infectious and posttraumatic OD groups (all $p < 0.05$).

Relationship of QOD scores to the demographic variables and olfactory function

The correlation results are shown in Table 2. Overall results showed that olfactory threshold ($r = -0.098$, $p = 0.012$, $n = 649$), olfactory discrimination ($r = -0.115$, $p = 0.003$, $n = 649$), olfactory identification ($r=-0.088$, $p=0.017$, $n=733$), TDI score ($r = -0.114$, $p = 0.003$, $n = 649$), self-assessed olfactory function ($r = -0.275$, $p < 0.001$, $n = 690$), disease duration ($r = -0.119$, $p = 0.001$, $n = 713$) and age ($r = -0.092$, $p = 0.012$, $n = 733$) were negatively associated with the QOD-QOL score (Figure 2). The QOD-QOL scores in females were higher than that in males ($p < 0.05$). The QOD-QOL scores in younger patients who were less than 60 years old were higher than that in older patients (younger: 21.02 ± 11.59; older: 18.98 ± 10.32; $t = 2.49$, $p < 0.05$). In addition, the QOD-QOL scores in anosmic patients (21.17 ± 11.65) were higher than that in normosmic patients (19.47 ± 10.43) ($p < 0.05$), but similar with that in hyposmic patients (16.88 ± 10.34) ($p > 0.05$) (Figure 1). Olfactory discrimination ($r = 0.118$, $p = 0.003$, $n = 649$), olfactory identification ($r = 0.110$, $p = 0.003$, $n = 733$), TDI score ($r = 0.119$, $p = 0.002$, $n = 649$), and disease duration ($r = -0.187$, $p < 0.001$, $n = 713$) were associated with the QOD-P score. The self-assessed olfactory function ($r = -0.336$, $p < 0.001$, $n = 429$) and disease duration ($r = -0.101$, $p = 0.037$, $n = 429$) were negatively associated with the QOD-VAS score.

Factors influencing QOD-QOL, QOD-P and QOD-VAS

To investigate the factors influencing QOD-QOL, QOD-P and QOD-VAS separately, we used three separate hierarchical regression analyses. All of them were conducted by entering sociodemographic variables (sex, age and disease duration) in the first step, disease causes in the second step, TDI scores in the third step and self-assessed olfactory function entered in the final step. Hierarchical regression analyses results are shown in Table 3.

With QOD-P as outcome measure, sociodemographic variables (sex, age and disease duration) explained 4.6% of the variance ($F = 10.60$, $p < 0.001$) in the first model. Sex and disease duration

Table 3. Hierarchical multiple regressions for general factors and QOD.

Model	Factors	QOD-P		QOD-VAS		QOD-QOL	
		β	P	β	P	β	P
Model 1	Sex	-0.12	**<0.01**	-0.10	0.054	-0.07	0.07
	Age (years)	-0.01	0.84	0.02	0.68	-0.08	0.06
	Duration (years)	-0.18	**<0.01**	-0.11	**0.049**	-0.13	**<0.01**
	Adjusted R^2	0.046		0.018		0.024	
	F	**10.60*****		**3.04***		**5.90****	
Model 2	Sex	-0.10	**0.02**	-0.07	0.22	-0.05	0.20
	Age (years)	0.01	0.81	0.04	0.46	-0.05	0.26
	Duration (years)	-0.14	**<0.01**	-0.01	0.87	-0.09	**<0.05**
	Sinonasal	0.02	0.86	0.28	**0.03**	0.06	0.57
	Post-infectious	0.19	0.27	0.43	**0.03**	0.21	0.23
	Post-traumatic	0.13	0.31	0.27	0.08	0.20	0.13
	Idiopathic	0.01	0.97	0.15	0.41	0.01	0.94
	Neurodegenerative	-0.04	0.42	-0.02	0.77	-0.05	0.30
	Adjusted R^2	0.071		0.070		0.061	
	Adjusted R^2 change	0.025		0.052		0.037	
	F change	**4.20****		**4.80*****		**5.62*****	
Model 3	Sex	-0.09	**0.04**	-0.08	0.12	-0.07	0.10
	Age (years)	0.03	0.50	0.02	0.68	-0.07	0.10
	Duration (years)	-0.14	**<0.01**	-0.03	0.69	-0.10	**0.04**
	Sinonasal	-0.01	0.91	0.30	**0.02**	0.10	0.36
	Post-infectious	0.13	0.46	0.48	**0.02**	0.28	0.10
	Post-traumatic	0.12	0.36	0.27	0.08	0.21	0.10
	Idiopathic	-0.05	0.76	0.18	0.32	0.08	0.64
	Neurodegenerative	-0.05	0.30	-0.01	0.90	-0.04	0.44
	TDI	0.10	**0.02**	-0.11	0.053	-0.12	**<0.01**
	Adjusted R^2	0.079		0.077		0.072	
	Adjusted R^2 change	0.008		0.007		0.011	
	F change	**5.85***		3.77		**8.34****	
Model 4	Sex	-0.09	**0.03**	-0.09	0.07	-0.08	**0.04**
	Age (years)	0.04	0.38	0.04	0.49	-0.05	0.28
	Duration (years)	-0.14	**<0.01**	-0.04	0.53	-0.1	**0.03**
	Sinonasal	-0.002	0.99	0.33	**0.01**	0.13	0.22
	Post-infectious	0.13	0.45	0.50	**0.01**	0.29	0.08
	Post-traumatic	0.12	0.35	0.27	0.06	0.22	0.09
	Idiopathic	-0.04	0.84	0.24	0.17	0.13	0.44
	Neurodegenerative	-0.05	0.30	-0.01	0.92	-0.04	0.42
	TDI	0.14	<0.01	0.04	0.47	-0.02	0.62
	SA	-0.08	0.07	-0.34	**<0.01**	-0.24	**<0.001**
	Adjusted R^2	0.082		0.165		0.115	
	Adjusted R^2 change	0.003		0.088		0.043	
	F change	3.23		**35.95*****		**29.72*****	

QOD-P: Questionnaire of Olfactory Disorders-parosmia; QOD-QOL: Questionnaire of Olfactory Disorders-quality of life; QOD-VAS: Questionnaire of Olfactory Disorders-visual analog scales; TDI: total score of the olfactory threshold, discrimination and identification tests; SA: self-assessment of olfactory function; * P<0.05; **P<0.01; ***P<0.001.

made a significant contribution to the model (Sex: β = -0.12, p < 0.01; duration: β = -0.18, p < 0.01). After controlling for sociodemographic variables (sex, age and disease duration), the disease causes explained additional 2.5% of variance in the second model (F change = 4.20, p < 0.01). Furthermore, after controlling the sociodemographic variables and disease causes, TDI scores explained an additional 0.8% of the variance (F change = 5.85, p < 0.05). After controlling the sociodemographic variables disease causes, and TDI scores, no significant influence of self-assessed olfactory function on QOD-P was found in the final model (F change = 3.23, p > 0.05).

With QOD-QOL as outcome measure, sociodemographic variables (sex, age and disease duration) explained 2.4% of the variance (F = 5.90, p < 0.01) in the first model. Disease duration made a significant contribution to the model (duration: β = -0.13, p < 0.01). After controlling for sociodemographic variables (sex, age and disease duration), the disease causes explained additional 3.7% of variance in the second model (F change = 5.62, p < 0.01). Furthermore, after controlling the sociodemographic variables and disease causes, TDI scores explained an additional 1.1% of the variance (F change = 8.34, p < 0.01). In the final model, self-assessed olfactory function explained an additional 4.3% of variance (F change = 29.72, p < 0.001) after excluding the impact of factors in Model 3.

With QOD-VAS as outcome measure, sociodemographic variables (sex, age and disease duration) explained 1.8% of the variance (F = 3.04, p < 0.05) in the first model. Disease duration made a significant contribution to the model (duration: β = -0.11, p < 0.05). After controlling for sociodemographic variables (sex, age and disease duration), the disease causes explained additional 5.2% of variance in the second model (F change = 4.80, p < 0.01). Furthermore, after controlling the sociodemographic variables and disease causes, TDI scores explained no additional variance on QOD-VAS (F change = 3.77, p > 0.05). In the final model, self-assessed olfactory function explained an additional 8.8% of variance (F change =35.95, p < 0.001) after excluding the impact of factors in Model 3.

Discussion

To the best of our knowledge this is the largest study looking at olfactory-related QOL in OD patients. The results showed that the poor olfactory-related QOL is most pronounced in younger female patients with post-infectious and posttraumatic OD, with poorer olfactory function, and with shorter disease duration. Additionally, the poor olfactory-related QOL is least pronounced in older male patients with sinonasal or idiopathic OD, with better olfactory function, and with longer disease duration.

The present study demonstrated poorer olfactory-related QOL in patients with OD regardless of causes than in healthy controls, which is consistent with previous studies[14,15,20,21,24]. In addition, we found that except for the idiopathic group, the QOD-P in the sinonasal, post-infectious and post-traumatic patient groups was higher than in healthy controls. Our findings demonstrated that demographic, disease factors and olfactory dysfunction influenced the QOD values.

Disease duration was negatively correlated with QOD-P, QOD-QOL and QOD-VAS scores. With regard to parosmia, the results were partly consistent with the findings of Frasnelli and Hummel[13], who reported that the duration of the OD in patients with parosmia was shorter compared to OD patients without parosmia. In addition, previous studies showed that parosmia in OD patients would reduce gradually over time, even after several years [25] which is in line with our QOD-P findings.

In contrast to previous findings that the disease duration had no influence on the QOD scores[13,26], the QOD-QOL and QOD-VAS in patients were also getting better gradually over time in the present study, which may be interpreted as adjustment. Croy et al.[27]. showed that patients with OD who had it for 1 year or longer tended to use their olfaction less than those who had it for less than 1 year.

Compared to male OD patients, female patients showed better olfactory function, but presented poorer QOD-P, QOD-QOL and QOD-VAS, which is consistent with previous study results[13,28]. These findings may be interpreted in this way that olfaction is more important to females than males, and that olfactory dysfunction may be much more meaningful to females than males. Thus, females may have more complaints due to olfactory dysfunction because it has a greater impact on their lives. Furthermore, patients with post-infectious and post-traumatic OD showed poorer QOD-P, QOD-QOL and QOD-VAS than patients with sinonasal and idiopathic OD. The results were partly consistent with the findings of Jung, Lee, and Park[29]. who reported that patients with post-infectious OD showed a more depressive mood than those with sinonasal OD. The results of hierarchical regression analyses also demonstrated that disease cause was a significant predictor of QOD-P, QOD-QOL or QOD-VAS, after adjustment for sex and disease duration. With regard to parosmia, previous studies showed that parosmia did not commonly occur in patients with sinonasal OD, but more often in patients with post-infectious and post-traumatic OD[30]. The differences in QOD-QOL and QOD-VAS may be attributed to the fact that post-infectious and post-traumatic OD usually start abruptly and do not present with fluctuations in olfactory ability, whereas sinonasal OD progresses slowly[18] which might enable patients to adapt and cope with the situation.

Finally, olfactory function was found to be associated with QOD-P, QOD-QOL and QOD-VAS in the present study, which is in line with previous studies[20,21,24]. Interestingly, the results of hierarchical regression analyses showed that self-assessment of olfactory function explained more of the variance in QOD-QOL and QOD-VAS than the olfactory function evaluated by Sniffin' Sticks test which could explain the often-observed discrepancy between

objective and subjective olfactory impairment. In contrast, only the olfactory function evaluated by Sniffin' Sticks test, but not the self-assessed olfactory function, was a significant predictor of QOD-P. The obviously better correspondence between self-assessment and QOL than between measured values and QOL could thus indicate a greater significance of self-assessment in olfactory dysfunction. However, this must be viewed with caution, as different parameters are measured with different indications. While the subjective evaluation is highly important for the patients´ well-being, the measured olfactory function is highly important for therapy decisions and predicts the success of the therapy[31-33]. In practice, both parameters should therefore be recorded in order to characterize the severity of the olfactory disorder from both a patient and a medical perspective. As a limitation of the study, the unequal group sizes of the individual diagnoses of OD can be seen.

Conclusion

This multicenter study using an OD-specific questionnaire to evaluate QOL in a large sample shows that OD deeply influences the daily life in patients. Several factors such as disease cause, disease duration, sex, or self-assessed olfactory function have an independent impact on the olfactory-related QOL of patients. This might explain differences in QOL in patients with objectively identical olfactory measurements and should be taken into account when assessing the individual severity of OD in addition to the psychophysical testing results.

Authorship contribution

LZ: data analysis and interpretation; drafting, revision, and final approval of the manuscript; TH: study conception; data acquisition and interpretation; revision, and final approval of the manuscript; MO, TB, GB, CM, AW, CO, ÖG, SN: data acquisition; revision, and final approval of the manuscript; SL: data analysis and interpretation; revision and final approval of the manuscript; AH: study conception; data acquisition and interpretation; revision and final approval of the manuscript

Conflict of interest

No conflict of interest.

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