

TITLE: Quality of life impairment and its assessment in patients with olfactory dysfunction, a narrative review

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Abstract

Introduction: Olfactory dysfunction (OD) is a frequent medical condition which might determine an important reduction of the patient's quality of life (QoL). The analysis of OD-related QoL may play an important role in clinical practice since the patient's perspectives may influence clinical decisions and could be used to monitor the longitudinal course of individual outcomes.

Evidence acquisition: Only a limited number of specific instrument able to evaluate OD-related QoL have been proposed so far and their clinical application is limited. The aim of this review was to analyze the available instruments useful for OD-related QoL measurement in order to increase clinicians' awareness of OD and their ability to evaluate its impact.

Evidence synthesis: The Questionnaire of Olfactory Disorders (QOD) is the more widely used but its internal consistency is poor. The Importance of Olfaction Questionnaire demonstrated a good internal consistency but no information regarding its reliability are available. The Self-Administered Odor Questionnaire (SAOQ) demonstrated satisfactory clinical validity and responsiveness to changes but no information regarding its internal consistency and reliability are available. The Scandinavian adaptation of the Multi-Clinic Smell and Taste Questionnaire (MCSTQ-Sc) appears too time consuming. Finally, the Modified Short version of the QOD (MS-QOD) demonstrated satisfactory internal consistency, optimal test re-test reliability and satisfactory discriminant and convergent validity.

Conclusions: There is a need for a psychometrically robust, time- and cost-efficient, easy-to-use instrument to be used in everyday clinical practice for the evaluation of the impact of OD on patient's QoL

Key words: olfactory; quality of life; self-assessment; nose

TEXT

Introduction

Olfactory dysfunction (OD) can be classified as either quantitative, involving alteration in the strength but not in the quality of odors, or qualitative, in which the quality of odors is changed¹. OD can affect up to one fifth of the general population² and about the 60% of individuals over 65 years³. The high prevalence of OD is not surprising since numerous reasons could determine an impairment of the olfactory function, including congenital causes (characterized by an hypoplastic or aplastic olfactory bulb)^{4,5} and acquired ones, such as damage to the olfactory epithelium due to trauma, drugs or toxins; age-related impaired ability to regenerate olfactory neurons; reduced release of odor molecules due to impaired chewing; upper airways infections; sinonasal, psychiatric, and neurological diseases (for example Parkinson's disease)⁶⁻¹¹. Despite the high prevalence of OD, the frequency of self-reported smell loss varies between 1.4% and 15%¹². This discrepancy might be related to several causes. First of all, olfactory information is processed unconsciously to a relatively large extent. Probably for this reason, unawareness of olfaction loss is not uncommon. In addition, symptomatic patients often report difficulties in finding and receiving the appropriate level of care. Landis¹³ found that, among 230 patients visiting a smell and taste clinic, 80% of the patients visited on average 2.1 ± 0.1 other physicians before visiting this clinic and 60% of patients received unsatisfactory information about their disorder.

The ENT surgeons seem to have a central role in addressing OD because of their confidence with nasal pathologies and the availability of diagnostic instruments (such as the nasal endoscopes) able to visualize the olfactory cleft and to detect nasal pathologies that could be associated with OD¹³. However, ENT examination should be paired with both objective and subjective olfactory assessments. In particular, the subjective measurements seem particularly useful since neither the electrophysiological assessment, nor the function imaging or the psychophysical tests¹⁷ can quantify the level of handicap that patients experience as a result of their OD. In fact, OD decreases the ability to identify hazards and may limit several daily life functions (food intake, safety, personal hygiene, and sexual life) with a consequent reduction of the patient's quality of life (QoL)^{12, 14-16}.

The measurement of QoL modifications related to OD may play an important role in clinical practice, since the patient's perspectives may influence clinical decisions. In addition, QoL assessment and patient's reported symptoms could be used to monitor the longitudinal course of individual outcomes. However, the best method to assess the OD-related QoL is still a matter of debate. This datum is probably related to the fact that the QoL in patients with OD appears to be related to several factors, such as the characteristics of OD (for example QoL in patients with phantosmia or parosmia seems to be affected even more than in patients with hyposmia¹²) and the effectiveness of coping strategies¹⁸.

In addition, the modification of QoL might be confounded by the presence of comorbidities or by the effect of the disease that finally lead to the OD. For example, in patients with olfactory loss secondary to chronic rhinosinusitis (CRS), the sinonasal disease itself has a negative impact on QoL^{15, 19, 20}. In order to overcome these problems, a few instruments specifically designed to evaluate the OD-related QoL have been developed so far¹². Unfortunately, their application in the clinical practice is limited and there is still disagreement about the best instrument available.

The aim of this narrative review is to evaluate the consequences of OD on QoL and to analyze the available instruments useful for its measurement in order to increase clinicians' awareness of OD and their ability to evaluate its impact. The underlying hypothesis is that a deeper knowledge of the available instruments for the OD-related QoL assessment might facilitate their application in the clinical practice, thus improving clinicians' ability to correctly evaluate the impact of OD, the course of the disorder, and the efficacy of possible therapies.

Consequences of OD on QoL

Olfaction plays a major role in guiding our attention towards hazards and towards items with positive connotations (for example food), it is involved in food intake, social communication and reproductive behaviors (such as emotional contagion, mate selection, inbreeding avoidance, in addition it could also influence the working abilities)²¹.

Difficulties in detection personal hazards, such as gas, smoke and spoiled food are frequently reported by patients with OD²¹. In particular, Miwa et al.¹⁴ who analysed retrospectively 420 patients with OD, reported that 25% of subjects enjoyed life less than before the disorder onset and that the detection of spoiled food and gas leak were the most commonly cited activities impaired by OD. As far as it is concerned the food intake, eating related difficulties are often reported by patients with OD²². The taste of food is strongly determined by olfactory experience, and a lack of the sense of smell consequently reduces the richness of food perception. This could lead to an alteration of eating behavior. In particular, Blomqvist et al.²³ who analyzed 72 patients with anosmia or hyposmia, found reduced appetite in 32% of them. Temmel et al¹⁸, who studied a population of 278 patients with OD, reported a reduction of appetite in 56% of them. On the other hand, other authors reported that 3-20% of patients with OD eat more²². Even if it is unclear why some patients with OD eat either less or more, OD seems to affect eating behavior in a large percentage of these patients. Food preparation could also represent a difficult task in patients with OD. In particular Miwa et al.¹⁴ reported that 49% of patients with OD have problem with cooking, mainly related to difficulties in detecting spoiled food. Personal hygiene is another common problem in patients with OD. In particular, Nordin et al¹⁶ who analyzed 50 patients with smell loss and with nasal polyposis and asthma found that 36% of

them were less aware of their personal hygiene, while worry about not being able to perceive the own body odor was reported by 41% of the patients in the study of Temmel et al.¹⁸. Probably related with insecurity about personal hygiene, patients with OD might also experience impairment in social relations and sex life. Gudziol et al.²⁴ demonstrated a significantly reduced sexual appetite as a consequence of OD. Moreover, Croy et al.²⁵ demonstrated that men born without a sense of smell described a reduced number of sexual relationships.

Finally, as far as it is concerned the working abilities, Nordin et al.¹⁶ reported a reduced working ability in 8% of patients with OD. Haxel et al.²⁶, who analysed a group of 105 dysosmic patients, reported that about two thirds of subjects needed additional arrangements during working life and 6% of the patients were forced to discontinue their profession because of OD.

Instrument for QoL evaluation in patients with OD

QoL measurements may play an important role in clinical practice, since the patient's perspectives may influence clinical decisions. In addition, QoL assessment and patient's reported symptoms could be used to monitor the longitudinal course of individual outcomes. In order to evaluate the patient's perspectives, it would seem to be easiest to ask the patients to simply rate the degree of their complaints. However, this approach appears problematic since previous reports suggested that self-assessment was less reliable than psychophysical testing both in healthy and in patient populations^{27, 28}. Temmel et al.¹⁸ reported in their study a 4% of patients with referred normal olfactory function despite the presence of an objective olfactory deficit. Nordin et al.²⁹ who analysed a group of 172 patients with a verified olfactory loss reported that 70% of them did not recognize their smell disorder. In addition, Landis²⁷ showed that, in healthy subjects, subjective olfactory ratings were not significantly correlated with the results of psychophysical testing. Similarly, a study on olfactory testing in patients with rhinological complaints demonstrated poor correlation between subjective smell loss and results of psychophysical assessment²⁸.

Since self-assessment seems to be unreliable, other authors used validated questionnaires in order to estimate the OD-related QoL. Typical questionnaires used to assess general QoL are the Short Form-12 and Short Form-36 health surveys³⁰, and the 90-item Symptom Checklist³¹. However, clinicians should pay attention using these questionnaires because it is difficult to determine whether a QoL modification is related to the OD or to the presence of comorbidities. For example, in patients with CRS (which frequently complain also OD) the sinonasal disease itself as well as the presence of comorbidities such as asthma and allergies might reduce both general and OD-related QoL^{34,35}. In addition, also other factors may affect the perceived QoL. Temmel et al.¹⁸, who studied 151 anosmic and 127 hyposmic patients, reported that the percentage of participants reporting a decrease in QoL

differed according to the cause of OD and that younger patients had the highest degree of difficulties, while women mentioned more complaints than men. Neuland et al.³⁶ found that patients with congenital anosmia indicated no loss (0%) in QoL, while acquired hyposmia affected QoL more than acquired anosmia. Croy et al.³⁷ reported that patients with OD duration of more than 1 year tended to use their sense of olfaction less often than patients with shorter disorder duration, indicating adjustment.

In order to provide a more reliable OD-related QoL evaluation, a few specific questionnaires have been developed so far (Table 1). One of the more widely used is the Questionnaire of Olfactory Disorders (QOD) developed by Frasnelli and Hummel²¹. It consists of 52 items that can be divided into three domains: 39 “negative” statements (NS, measuring the degree to which patients suffer from OD), 5 “positive” statements (PS, indicating the patient’s ability to cope with OD) and 8 “socially desired” statements (DS, indicating whether patients give answers that they believe they are expected to give). Patients could agree (2 points), partly agree (1 point) or disagree (0 points) with each statement. The internal consistency of QOD ranged from 0.54 (for the PS domain) to 0.93 (for the NS domain), while test-retest reliability ranged from 0.71 (for the NS domain) to 0.78 (for the PS domain). The clinical validity of QOD was evaluated by comparing the QOD results obtained in normal, hyposmic and anosmic patients. The results suggested that the results of the NS domain were different among these three group of patients. The QOD has been used in outcome researches: Mattos et al.³³ who studied 109 patients with CRS and OD, reported that non-white race, depression and worse SNOT-22 scores correlated with worse QOD scores, demonstrating how this questionnaire is a feasible tool for olfaction screening. Katotomichelakis et al.³⁸ focused on the effects of symptoms resolution in CRS after surgery and allergic rhinitis (AR) after immunotherapy, highlighting how restoring the olfaction was significantly associated with patients’ QoL and psychological state recovery. Even if widely used, the disappointing internal consistency of the PS domain of QOD imposed a modification of this questionnaire. For this reason, a modified short version of the QOD was developed (MS-QOD)³⁹. It consists of 25 statements divided into three general domains: 17 negative statements (QOD-NS), two positive statements (QOD-PS), and six socially desired statements (QOD-SD). The MS-QOD demonstrated satisfactory internal consistency, optimal test re-test reliability and satisfactory discriminant and convergent validity. Nonetheless, its application in outcome researches is still limited.

Croy et al.⁴⁰ developed the Importance of Olfaction Questionnaire. It consists in 18 four-scaled items, formulated as a personal statement, divided into three subscales: Association (reflecting the emotions, memories, and evaluations that are triggered by the sense of smell), Application (analyzing how much a person uses the sense of smell in daily life), and Consequence (focused on the importance of the

sense of smell in daily decisions). The questionnaire demonstrated a good internal consistency. Takebayashi et al.⁴¹ developed the self-administered odor questionnaire (SAOQ) which comprises 20 smell-related items (for example steamed rice, miso, seaweed, soy sauce etc.) scored using a 0-2 scale. The total score is expressed as percentage of proportion of the total score for each item compared with the full score. The SAOQ demonstrated satisfactory responsiveness to change, significant associations with the olfactometer results in patients with olfactory disorders and a sensitivity of 99.0% and a specificity of 90.1% using a cutoff value of 66.7% of the SAOQ score. Pusswald et al.⁴² developed the 12-item questionnaire for the assessment of self-reported olfactory functioning and OD-related QoL (ASOF). It includes 3 scales: subjective olfactory capability (1 item), self-reported smell-related problems (5 items), and olfactory-related quality of life (6 items). The questionnaire demonstrated satisfactory internal consistency and clinical validity. Nordin et al.⁴³ developed the Scandinavian adaptation of the Multi-Clinic Smell and Taste Questionnaire (MCSTQ-Sc). It consists of 14 questions about medical history, 24 questions about olfactory dysfunction, and 5 questions about the consequences of olfactory dysfunction. The questionnaire demonstrated good to excellent reliability but it appears to be time consuming.

Even if these instruments demonstrated satisfactory psychometric characteristics, their application in the clinical practice is still limited and the majority of them are available only in the English language. In addition, only scarce information regarding their responsiveness to changes are available.

Conclusions

Olfaction plays a pivotal role for food selection, social communication and harm avoidance. About one-fifth of the population exhibits smell disorders, most of them are not aware of it, and those who seek medical treatment often have problems finding a physician who is familiar with smell disorders¹². About one-fourth to one-third of patients presenting OD complain a noticeable reduction in QoL¹². The latter should be assessed using psychometrically validated instruments specifically developed in order to evaluate the Od-related QoL. Generic questionnaires, in fact, are too nonspecific to detect the direct influence of OD on daily life. A few specific questionnaires are available so far but their use in clinical practice is limited. This could be related to different causes. Some of these instruments are time consuming (for example the MCSTQ-Sc) while others appear not psychometrically robust (for example the positive subscale of the QOD). Moreover, the majority of these instruments are not available in languages different from English, thus reducing their applicability. There is a need for a psychometrically robust (with satisfactory internal consistency, reliability, clinical validity and responsiveness to changes), time- and cost-efficient, easy-to-use instrument to be used in everyday clinical practice for the evaluation of the impact of OD on patient's

QoL. In the absence of such an instrument it appears very difficult to correctly evaluate the impact of OD, the course of the disorder, and the efficacy of therapy.

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Table 1: Comparison among different questionnaires specifically designed in order to evaluate the QoL modification in OD patients. The results of Internal consistency (assessed through Cronbach's alpha coefficient), test-retest reliability and validity are reported as well as the number of items composing each questionnaire. NS = negative statements of the QOD; SF-36 = short form 36; BDI = Beck Depression Inventory

Questionnaire	Item	Internal consistency	Test-retest	Validity
Questionnaire for Olfactory Dysfunction (QOD) ²¹	52	0.54-0.93	0.71-0.78	Significant differences in the QOD-NS scores among anosmic, hyposmic and normosmic patients
Importance of Olfaction Questionnaire ⁴⁰	18	0.77	NT	NT
Self-administered odor questionnaire (SAOQ) ⁴¹	20	NT	NT	Significant correlations between SAOQ scores and olfactometer results
Assessment of self-reported olfactory functioning (ASOF) ⁴²	12	0.87-0.89	NT	Significant correlations between ASOF scores and objective olfactory tests

Multi-Clinic Smell and Taste Questionnaire for Scandinavian use (MCSTQ-Sc) ⁴³	43	NT	Good- excellent	NT
Short modified version of QOD (MS-QOD) ³⁹	25	0.91	0.99	Significant correlation between MS-QOD scores and SF-36 and BDI scores Significant differences in the MS-QOD scores among anosmic, hyposmic, and normosmic patients

NT = not tested