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Rhinology

Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD)

Versione italiana del brief Questionnaire of Olfactory Disorders (Brief-IT-QOD)

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SUMMARY

Objective. To evaluate the reliability and validity of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD).

Methods. The study consisted of six phases: item generation, reliability analysis (112 dysosmic patients for internal consistency analysis and 61 for test-retest reliability analysis), normative data generation (303 normosmic subjects), validity analysis (comparison of Brief-IT-QOD scores of healthy and dysosmic subjects and scores correlation with psychophysical olfactory testing TDI and SNOT-22 scores), responsiveness analysis (10 dysosmic chronic rhinosinusitis with nasal polyps patients before and after biologic therapy), and cut-off value determination (ROC curve analysis of Brief-IT-QOD sensitivity and specificity).

Results. All subjects completed the Brief-IT-QOD. Internal consistency ($\alpha > 0.70$) and test-retest reliability (ICC > 0.7) were acceptable and satisfactory for both questionnaire subscales. A significant difference between dysosmic and control subjects was found in both subscales ($p < 0.05$). Significant correlations between subscales scores and TDI and SNOT-22 scores were observed. Brief-IT-QOD scores before treatment were significantly higher than after biological therapy.

Conclusions. Brief-IT-QOD is reliable, valid, responsive to changes in QoL, and recommended for clinical practice and outcome research.

KEY WORDS: olfaction disorders, questionnaire, quality of life

RIASSUNTO

***Obiettivo**. Valutare affidabilità e validità della versione italiana del Questionario Breve dei Disordini Olfattivi (Brief-IT-QOD).*

***Metodi**. Lo studio è stato composto da sei fasi: generazione del questionario, analisi di affidabilità (112 pazienti disosmici per la consistenza interna e 61 per l'affidabilità test-retest), generazione di dati normativi (303 soggetti normosmici), analisi di validità (comparazione dei punteggi Brief-IT-QOD di pazienti e controlli e correlazione con valutazione olfattoria psicofisica TDI e punteggio SNOT-22), analisi di responsività (10 pazienti disosmici con rinosinusite cronica poliposica prima e dopo terapia biologica), e determinazione di valori soglia.*

***Risultati**. Tutti i soggetti hanno completato il Brief-IT-QOD. Consistenza interna ($\alpha > 0,70$) e affidabilità test-retest (ICC > 0,7) erano soddisfacenti per entrambe le sottoscale del questionario. In entrambe le componenti è stata rilevata una differenza significativa ($p < 0,05$) fra individui disosmici e normosmici. Sono emerse correlazioni significative fra i punteggi delle sottoscale e i punteggi TDI e SNOT-22. I punteggi al Brief-IT-QOD erano significativamente più alti prima della terapia con farmaco biologico.*

***Conclusioni**. Il Brief-IT-QOD è affidabile, valido, responsivo ai cambiamenti nella qualità di vita e raccomandato per pratica clinica e ricerca.*

PAROLE CHIAVE: *disturbi dell'olfatto, questionario, qualità di vita*

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Introduction

Olfactory dysfunction (OD) is defined as the reduced or distorted ability to smell during sniffing or eating. It can be classified as either quantitative, involving alteration in the strength but not in the quality of odour perception (hyposmia, anosmia), or qualitative, in which the quality of odour perception is changed (parosmia, phantosmia) [1]. The prevalence of OD in the general population is estimated to be 3%-5% for total smell loss (anosmia) and 15%-25% for partial impairment (hyposmia); this increases to about 60% in individuals older than 65 years [1]. OD has profound effects on quality of life (QoL), physical and social function and even mortality [2,3]. In their review on olfactory disorders and QoL, Croy et al. [2] showed that loss of the sense of smell causes disturbances in important areas of daily life. The main issues regarded food intake (increased/decreased quantities, decreased enjoyment, decreased appetite, difficulties in cooking), safety (eating spoiled food, failure to perceive fire, smoke, or gas), personal hygiene, social life, household chores and working life. Patient-reported worries about these different aspects and consequent daily-life restrictions negatively affected QoL [2].

In order to provide a proper assessment of this frequent disorder, it is important to measure and monitor the impact of OD on patients' QoL. Questionnaires are the preferred means for evaluation of this aspect and are often used as outcome measures. The Questionnaire of Olfactory Disorders (QOD) [4] was developed by Frasnelli and Hummel as a self-report inventory to assess subjective information on OD. The QOD consists of several items that can be divided into three subscales (Parosmia, Quality of Life, Socially-desired) and one 5-item visual analogue scale.

Because of its excellent psychometric properties, the QOD has been widely used in clinical settings and has been translated into several languages [5-8]. However, the length of the questionnaire can be overwhelming for patients, thus limiting its application as an evaluation tool both in the clinic and in research. The literature supports the use of shorter and simpler versions of questionnaires, which favour greater response rates and higher quality of data [9].

Attempts have been made to address this issue. In 2019, Mattos and colleagues [10] developed a brief version of the "negative statements" QOD domain (QOD-NS). This is made up of only 7 items, but maintains consistency in measured patient-reported outcomes of olfactory-specific QoL. Later, Zou et al. [11] created a brief version of the QOD (brief-QOD) which included Mattos' 7 items concerning QoL [10] (QOD-NS) plus 4 items regarding parosmia (QOD-P) and 3 visual analogue scales (QOD-VAS). The brief-QOD showed suitable reliability and validity to assess the subjective severity of OD. The availability of a valid and reliable instrument able to assess the QoL in patients with OD is useful in clinical practice, but an Italian version of this instrument is lacking.

The aim of this study was to validate the Italian version of the brief-QOD (Brief-IT-QOD) and to use it to evaluate the OD-related QoL in a group of Italian individuals. In particular, the specific aims of the study were to: (1) culturally adapt the brief-QOD into Italian, (2) evaluate the questionnaire's internal consistency and reliability, (3) provide normative data of the Italian population, (4) evaluate its validity and responsiveness, (5) calculate the cut-off score of this questionnaire.

The underling hypotheses are: (1) the brief-QOD can be culturally adapted into Italian; (2) the Italian version of the questionnaire presents strong internal consistency and reliability; (3) the validity and responsiveness of the Italian version of the brief-QOD are strong.

The importance of this study lies in the fact that a validated brief-QOD for the Italian language would be useful in clinical practice, for example during the assessment of patients suffering from nasal diseases, allowing better knowledge of OD-related QoL. Furthermore, a validated Italian brief-QOD could facilitate both the diagnostic work-up and the decision-making process on treatment options.

Materials and methods

The study consisted of six different phases: back-translation and cross-cultural adaptation into Italian of the brief-QOD (phase 1); internal consistency and reliability analysis (phase 2); normative data generation (phase 3); validity analysis (phase 4); responsiveness analysis (phase 5); cut-off value (phase 6). The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist was followed for the different phases [12].

Participants

Different groups of patients and controls were recruited for each of the six different phases of the study (Tab. I). Inclusion criteria were: normal cognitive function (Mini Mental State Examination score > 24 for subjects older than 65), preserved reading skills, age > 18 years, no history of neoplastic, airway, neurologic, rheumatologic, hematologic, or endocrinologic disorders.

Data for phases 2, 3, and 4 were obtained from different otorhinolaryngologic (ENT) centres in Italy to ensure applicability of the Brief-IT-QOD in different settings. All enrolled subjects underwent an objective nasal assessment which included a full head and neck examination and a nasal endoscopy (with specific assessment of olfactory cleft

Table I. Clinical and demographic characteristics of the samples.

Phase of the study		Type of study	Sample clinical characteristics	Mean age (range years)	Sex	
					M	F
1	Item generation	Item generation	Patients with OD (n = 20)	53.3 (42-78)	10	10
2	Internal consistency	Internal consistency	Patients with OD (n = 112)	57.6 (18-87)	53	59
	Reliability analysis	Test-retest reliability	Patients with OD (n = 61)	57.3 (20-82)	30	31
3	Normative data generation	Normative data	Asymptomatic subjects (n = 303)	54.9 (18-87)	141	162
4	Validity analysis	Clinical validity	Asymptomatic subjects (n = 303) Patients with OD (n = 112)	54.9 (18-87) 57.6 (18-87)	141 53	163 59
		Concurrent validity (correlation between Brief-IT-QOD and I-SNOT-22 scores)	Patients with OD (n = 112)	57.6 (18-87)	53	59
5	Responsiveness analysis	Comparison pre- and post-biological therapy	Patients with OD (n = 10)	52.2 (41-67)	7	3

Age is reported as mean (range). OD: olfactory dysfunction.

patency) using a 30° endoscope, 2.7 mm diameter. In addition, orthonasal olfactory performance was evaluated using the extended version of the Sniffing test (Burghart Messtechnik GmbH, Germany), a reliable, and validated psychophysical test able to evaluate olfactory threshold, discrimination, and identification (TDI) using pens filled with odourants [13]. The TDI score, which ranges from 1 to 48, was used to define functional anosmia (TDI ≤ 16), hyposmia (16 < TDI < 31), or normosmia (TDI ≥ 31) [14].

Phase 1: back-translation and cross-cultural adaptation into Italian of brief-QOD

A cross-cultural adaptation process of translation and back-translation was performed. Items of the original brief-QOD questionnaire were first translated into Italian by two bilingual otorhinolaryngologists experienced in olfactory disorders management (step 1: forward translation). Discussion of the translated text with two other otorhinolaryngologists with extensive experience in nasal diseases ensured the unanimity and the interpretation of the translated text (step 2: synthesis). Twenty patients, 10 males and 10 females, with a median age of 55.3 years (range 42-78), reporting hyposmia were enrolled in a pilot study (step 3: pilot study). OD was related to chronic rhinosinusitis with nasal polyps (CRSwNP) in all cases. Each patient autonomously filled in the first translation of the brief-QOD and discussed the wording and meaning of each item of the questionnaire with the senior clinician. The wording of the questionnaire was modified considering the suggestions given by patients (step 4: expert panel). This new and final version of the Italian brief-QOD (called Brief-IT-QOD, Tab. II) was then translated back into English by a qualified professional translator (step 5: backward translation). This back-translation was compared to the original text by the professional translator; no items of incongruent translation were noted as every item was semantically identical to the original English text. The professionals involved in the cross-cultural adaptation also discussed the original version, the final translation into Italian, and the back-translation. Finally, the readability of the Brief-IT-QOD was checked by a dedicated company. The text was considered readable by a person with the reading competence of five years of primary education.

Phase 2: internal consistency and reliability analysis

The aim of this phase was to assess the reproducibility of Brief-IT-QOD. This was evaluated with two methods: internal consistency and test-retest reliability. The first assesses the extent to which each item in a factor measures the same underlying construct, while the latter is obtained by administering the same test twice over a period of time to a group of individuals.

Clinical data were obtained from 112 patients (53 males and 59 females) evaluated for OD. The mean age of patients with OD was 57.6 ± 14.1 years (18-87 years). Eighteen were affected by functional anosmia, while the remaining 94 were hyposmic. The aetiology of OD was CRSwNP (60 patients), idiopathic (23 patients), viral infection (20 patients), and head trauma (9 patients). Internal consistency of Brief-IT-QOD was assessed using Cronbach's alpha coefficient. Values between 0.7 and 0.9 were taken to indicate acceptable internal consistency [15]. For this analysis, the Brief-IT-QOD scores obtained in the group of 112 patients were used.

Of the 112 patients involved in internal consistency analysis, 61 patients (30 males and 31 females) were randomly

Table II. Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD).

Il questionario seguente indaga il ruolo dell'olfatto nella sua vita quotidiana. Per favore, risponda sinceramente alle domande, non ci sono risposte giuste o sbagliate.

P1	A causa di problemi all'olfatto, gli alimenti hanno un sapore diverso da quello che dovrebbero avere.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
P2	Sento costantemente un odore spiacevole nel naso, a prescindere dalla prossimità di una fonte odorosa.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
P3	Odori che sono piacevoli per gli altri a me sembrano fastidiosi.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
P5	Il problema più grave per me non è di sentire meno odori o non poter sentirli in assoluto, ma il fatto che abbiano un profumo diverso da quello che dovrebbero avere.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL1	A causa dei disturbi all'olfatto vado più raramente al ristorante con parenti o amici.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL2	Temo che non riuscirò mai ad abituarmi a questo problema.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL3	Faccio fatica a rilassarmi a causa dei disturbi dell'olfatto di cui soffro	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL4	Mi sento isolato/a dalle altre persone per via delle difficoltà con l'olfatto.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL5	A causa dei disturbi dell'olfatto, mangio di più/di meno rispetto a prima.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL6	I disturbi dell'olfatto mi causano problemi nelle mie attività quotidiane.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐
QOL7	Le difficoltà con l'olfatto mi rendono nervoso/a.	D'accordo	☐
		Abbastanza d'accordo	☐
		Abbastanza in disaccordo	☐
		Totalmente in disaccordo	☐

selected for test-retest reliability analysis. For this purpose, the Brief-IT-QOD was distributed and filled in twice with a 2-week interval by patients. A variation of two days before or after the requested two weeks was accepted in case of patient's needs. A 2-week interval period was selected because no substantial change in olfactory abilities was expected to take place within this period. No access to answers given to the first questionnaire was granted to patients when filling in the second Brief-IT-QOD. Test-retest reliability was assessed through Internal Consistency Coefficient (ICC). Correlation strength was considered strong for values greater than 0.5, moderate for values ranging between 0.3 and 0.5 and weak for values less than 0.3 [16].

Phase 3: normative data

The aim of this phase was to establish the baseline distribution for Brief-IT-QOD scores in a representative sample of normosmic subjects with no history or symptoms of OD. In all, 303 asymptomatic control subjects, 141 males and 162 females, with a mean TDI score of 34.1 ± 2.6 (31-40) and no past medical history of sinonasal, neoplastic, airway, neurologic, rheumatologic, haematologic, or endocrinologic disorders were enrolled. The mean age of the normosmic subjects was 54.9 ± 17.6 years (range 18-87). Each subject managed to complete the Brief-IT-QOD without any help. The data obtained from this group of patients were also used for clinical validity analysis of phase 4 of the study. Four age categories were considered (18-40 years, 41-60 years, 61-80 years, and > 81 years).

Phase 4: validity

The aim of the 4th phase of the study was to assess the degree to which the Brief-IT-QOD measures the construct it purports to measure (validity) [17]. Construct validity was assessed by comparing the Brief-IT-QOD scores obtained in patients with OD and in normosmic subjects. In addition, in order to define a clinically relevant difference score for purposes of group comparisons, Cohen's effect sizes (ES) were calculated for each of the subscales of the Brief-IT-QOD. A clinically relevant difference score for the Brief-IT-QOD subscales to use in group comparisons was defined as an effect size of 0.50 or greater. Criterion validity evaluates the ability of the Brief-IT-QOD to adequately reflect olfactory-related QoL. However, since there is no instrument that is able to assess olfactory-related QoL validated into Italian, we decided to collect the Sino-Nasal Outcome Test-22 (I-SNOT-22) [18] scores (a questionnaire made of 22 CRS-related items which contains also a question related to OD) and to analyse their correlations with Brief-IT-QOD scores. In addition, the correlations between the Brief-IT-QOD scores and the results of the extended version of the Sniffing test were also evaluated.

Phase 5: responsiveness

To evaluate the ability of the Brief-IT-QOD to detect important changes over time in the construct to be measured, a novel cohort of 10 patients with OD due to recalcitrant CRSwNP was recruited. Individuals included in this group experienced a significant improvement in nasal condition and had a measured increase in olfactory abilities (at Extended Smell Test) after biological therapy with dupilumab. This is a monoclonal antibody that inhibits signalling of both IL-4 and IL-13, which are key cytokines in type-2 mediated inflammation. Dupilumab is administered subcutaneously for the treatment of adults with inadequately controlled CRSwNP and has been demonstrated to produce a rapid and sustained improvement in the sense of smell [19]. Each patient autonomously filled in the Brief-IT-QOD before and after 2 months of therapy.

Phase 6: cut-off value

The cut-off value of the Brief-IT-QOD was determined based on the sensitivity and specificity indicators of the questionnaire using the ''receiver operating characteristic'' (ROC) curve [20]. The latter represents the relationship between the sensitivity and the specificity of a test by determining the real value of these two categories. In other words, the efficiency of a test is determined by its ability to correctly identify both positive and negative cases. The maximum value of 1.0 for sensitivity and specificity indicates a test of maximum efficiency to evaluate its purpose.

Statistical analysis

Statistical tests were performed using SPSS 23 statistical software (SPSS, Inc., Chicago, IL). Kolmogorov-Smirnov test was used to test the normality of the distribution of Brief-IT-QOD scores among patients and healthy subjects. Since this test demonstrated that the distribution of the scores was normal in both groups, parametric tests were used. The internal consistency was assessed using Cronbach's alpha coefficient. ICC was used to evaluate the test-retest reliability of the Brief-IT-QOD by comparing baseline and retesting responses. The Anova test was used to evaluate the Brief-IT-QOD scores among the different age groups of asymptomatic subjects. Student's t-test was used to compare the results obtained in OD patients and in the control group. The effect size was calculated as the difference between the experimental group mean minus the control group mean, divided by the standard deviation of the control group [21]. The correlation between Brief-IT-QOD and I-SNOT-22 scores was assessed using Pearson test. The distribution of Brief-IT-QOD scores obtained in pre- and post-treatment evaluations were compared using the Mann-Whitney test. For all statistical comparisons an $\alpha = 0.05$ and a power of 0.80 were used.

Results

All patients and control subjects included in the study managed to complete the Brief-IT-QOD without needing assistance. The time required to fill out the questionnaire never exceeded 7 minutes.

Phase 2: internal consistency and reliability analysis

Internal consistency was satisfactory with a Cronbach alpha score of $\alpha = 0.78$ for the QOD-P subscale and $\alpha = 0.97$ for the QOD-NS subscale. In addition, the test-retest reliability was satisfactory for both the subscales with an ICC of 0.77 (0.71-0.86) for the QOD-P subscale and 0.91 (0.84-0.95) for the QOD-NS subscale.

Phase 3: normative data

The mean age of normosmic subjects (n = 303) was 54.9 years (18-87). Forty-seven percent of subjects were males. Mean Brief-IT-QOD scores corresponding to different age categories are reported in Table III. No significant differences among the four age categories of normosmic subjects were demonstrated on Anova test for either the QOD-P (p = 0.089) or QOD-NS (p = 0.271) subscales.

Phase 4: validity

For clinical validity analysis, the Brief-IT-QOD scores obtained in patients with OD were compared through Student's t test to the scores obtained by normosmic subjects. The results of this comparison are reported in Table IV. The test revealed a significant difference between the OD group and the control group for both the QOD-P and QOD-NS subscales. ES results are also reported in Table IV, showing a significant effect size for both subscales.

The correlation between Brief-IT-QOD and I-SNOT-22 scores obtained in the group of patients with OD was analysed for concurrent validity. Positive significant correlations were found between the I-SNOT-22 and QOD-P scores (r = 0.275, Fig. 1) and QOD-NS scores (r = 0.321, Fig. 2). In addition, significant correlations were also found between the extended version of the Sniffing test scores and QOD-P scores (r = -0.258, Fig. 3) and QOD-NS scores (r = -0.403, Fig. 4)

Phase 5: responsiveness

Brief-IT-QOD scores obtained by a group of 10 patients with OD due to recalcitrant CRSwNP, who referred a significant improvement of nasal condition and demonstrated an improvement in olfactory abilities measured by the Extended Smell Test after two months of biological therapy with dupilumab, were compared for responsiveness analysis (7 of 10 patients were anosmic before the beginning of the therapy and 3 of 10 patients were anosmic after two months of therapy). The mean QOD-P score in the pre-treatment condition was 5.7 ± 1.8, while the post-treatment score was 1.8 ± 1.6. Similarly, the mean QOD-NS score in the pre-treatment condition was 13.8 ± 1.3, while the post-treatment score was 4.3 ± 5.1. These differences were statistically significant (p = 0.001 and p = 0.001 respectively)

Table III. Mean ± standard deviation of Brief-IT-QOD subscales scores in asymptomatic subjects at different ages. Ranges are reported in parentheses.

	Age				
	18-40 (n = 73)	**41-60 (n = 113)**	**61-80 (n = 92)**	**> 81 (n = 25)**	**Total**
QOD-P	1.5 ± 2.3 (0-8)	1.3 ± 1.8 (0-6)	2.4 ± 2.6 (0-8)	2.4 ± 2.1 (0.8)	1.6 ± 2.2 (0-8)
QOD-NS	0.6 ± 1.7 (0-10)	0.2 ± 1.1 (0-7)	0.6 ± 1.9 (0-11)	0.6 ± 1.5 (0-7)	0.4 ± 1.6 (0-11)

Table IV. Mean ± standard deviation of the Brief-IT-QOD subscales scores in patients with OD and in asymptomatic subjects. Ranges are reported in parentheses. The results of Student's t test are reported as well as those of Cohen's effect size.

	Asymptomatic subjects (n = 303)	**Patients with OD (n = 112)**	**P score**	**Cohen's d**
QOD-P	1.6 ± 2.2 (0-8)	4.6 ± 3.4 (0-12)	P = 0.001	*D* = 2.793
QOL-QOD	0.4 ± 1.6 (0-11)	4.3 ± 5.1 (0-19)	P = 0.001	*D* = 2.986

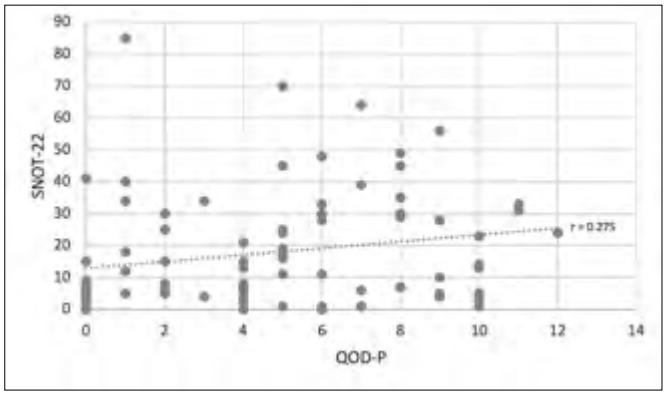

Figure 1. Correlation between the Parosmia subscale (QOD-P) scores of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD) and the Sino-Nasal Outcome Test-22 (SNOT-22). Tendency line with the correlation coefficient is also reported.

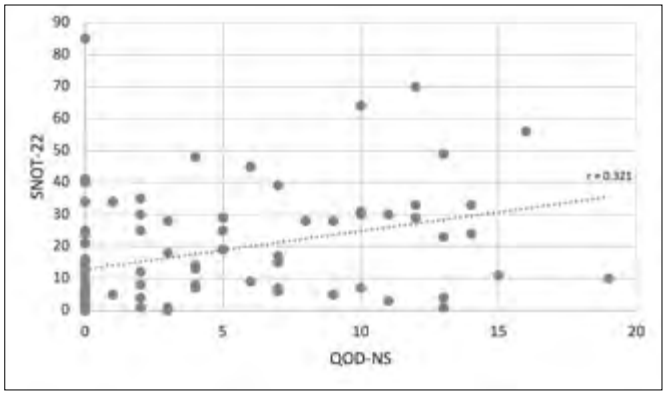

Figure 2. Correlation between the Negative Statement subscale (QOD-NS) scores of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD) and the Sino-Nasal Outcome Test-22 (SNOT-22). Tendency line with the correlation coefficient is also reported.

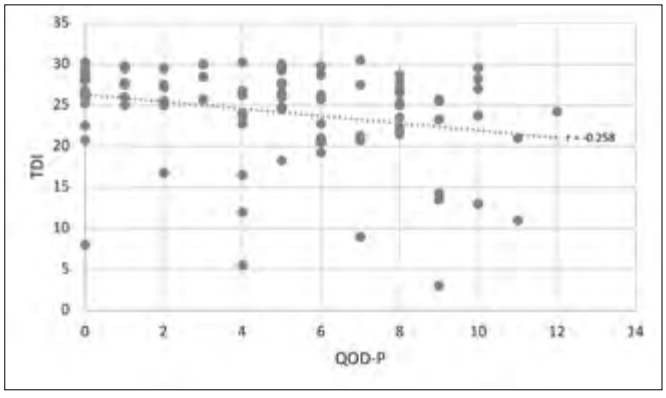

Figure 3. Correlation between the Parosmia subscale (QOD-P) scores of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD) and the extended version of the Sniffing test scores (TDI). Tendency line with the correlation coefficient is also reported.

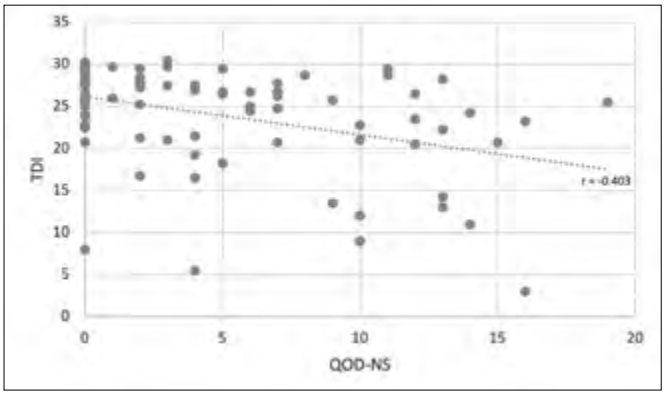

Figure 4. Correlation between the Negative Statement subscale (QOD-NS) scores of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD) and the extended version of the Sniffing test scores (TDI). Tendency line with the correlation coefficient is also reported.

using a Mann-Whitney test, suggesting a positive evolution of OD.

Phase 6: cut-off value

The comparison of the Brief-IT-QOD subscale scores obtained in patients with OD and in normosmic subjects demonstrated a significant difference between these two groups. Consequently, the samples could be submitted to ROC curve analysis, which allowed for determination of a cut-off value to discriminate the groups. In order to identify the Brief-IT-QOD cut-off value, the highest values of sensitivity and specificity were considered. The values of sensitivity and specificity for different Brief-IT-QOD subscale scores are reported in Table V, while the ROC graph is displayed in Figure 5. A QOD-P cut-off value of 3.5 demonstrated a sensitivity of 62.5% and specificity of 80.3%, while a QOD-NS cut-off value of 1.5 demonstrated a sensitivity of 55.4% and specificity of 86.6%.

Discussion

The QOD is a self-reported inventory that assesses QoL related to OD, initially developed in Germany and then adapted to different cultural and linguistic contexts, namely Chinese, Persian, Korean and English [4-8]. Mattos' brief version of the QOD-NS [10], on the other hand, was originally developed in English and has been translated and adapted into Spanish and French [22,23]. Zou's brief-QOD [11], comprising the 7 items of Mattos' QOD-NS [10] plus 4 items on parosmia and 3 visual analog scales, was created in English and not adapted to any other language. An Italian translation of the QOD, in any of its versions, is lacking.

In this study, the psychometric properties of the Brief-IT-QOD were analysed in a group of 112 patients with OD and

Table V. Coordinates of the ROC Curve for the cut-off. Value of the P-QOD and QOD-NS subscales of the Brief-IT-QOD.

	Cut-off value	Sensitivity	Specificity
P-QOD	-1,00	1.00	0
	0.50	0.813	0.528
	1.50	0.750	0.641
	2.50	0.670	0.669
	3.50	0.625	0.803
	4.50	0.509	0.859
	5.50	0.402	0.908
	6.50	0.304	0.972
	7.50	0.259	0.972
	8.50	0.152	1.000
	9.50	0.080	1.000
	10.50	0.027	1.000
	11.50	0.009	1.000
QOD-NS	-1,00	1.000	0
	0.50	0.571	0.817
	1.50	0.554	0.866
	2.50	0.464	0.894
	3.50	0.429	0.923
	4.50	0.375	0.944
	5.50	0.321	0.951
	6.50	0.295	0.965
	7.50	0.250	0.986
	8.50	0.232	0.986
	9.50	0.205	0.986
	10.50	0.152	0.993
	11.50	0.125	1.000

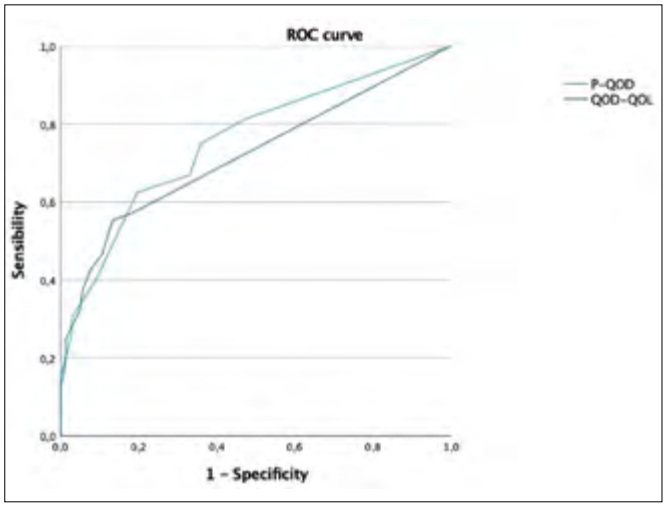

Figure 5. ROC curves of the Parosmia subscale (P-QOD) and Negative Statement subscale (NS-QOD) of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD) and the Sino-Nasal Outcome Test-22 (SNOT-22).

in a control group of 303 subjects. The results appear promising and seem to indicate that the Brief-IT-QOD can be applied in Italian patients with OD. In particular, all questionnaires were completely filled in, suggesting that all subjects understood the questions well and felt comfortable answering them. This allows to speculate that the Brief-IT-QOD is not a burdensome instrument, is easily self-administered, and can be quickly filled out.

The internal consistency of the Brief-IT-QOD appeared satisfactory, with the QOD-P subscale having an α of 0.78 and the QOD-NS subscale one of 0.97. The original study by Zou et al. [11] had Cronbach's α coefficients of 0.63 and 0.87 for QOD-P and QOD-NS, respectively, indicating an acceptable or excellent reliability. No other translation of this specific questionnaire is available in the literature, but our results for the QOD-NS subscale can be compared to those from Mattos' QOD-NS [10] and its adaptations. In fact, the French translation of QOD-NS (Fr-sQOD-NS) [2,3] had $\alpha = 0.96$, while the internal consistency of Chiesa-Estomba's Spanish version [22] measured with Cronbach α was 0.86.

As far as the reliability of the Brief-IT-QOD is concerned, the scores obtained in the test-retest analysis support the hypothesis that Brief-IT-QOD has high stability and reproducibility over time. In fact, ICC scores were 0.77 for the QOD-P subscale and 0.91 for the QOD-NS subscale. These values can be considered optimal both for group comparison and individual measurements over time. It is difficult to compare our results with the literature, as previous studies adopted different methods to evaluate reliability. The original study [11] used split-half reliability which was 0.60 and 0.87 for QOD-P and QOD-NS, respectively. The test-retest reliability of Fr-sQOD-NS [23] was high as well ($r = 0.88$, $p < .001$). Finally, the Spanish study [22] used the intraclass correlation coefficient to evaluate test-retest reliability and found a value of 0.85, which implies a high correlation.

To the best of our knowledge, no normative data on brief-QOD are available. In our sample, no difference in mean Brief-IT-QOD scores among the four age groups was observed. This supports the use of the test in patients with OD, regardless of their age. Our results of QOD-NS for normosmic subjects differ from those presented in the Fr-sQOD-NS study [23], with our cohort having lower average scores. However, comparison between the two studies is difficult, as the populations differ in age and numerosity. Furthermore, Leclercq and colleagues [23] do not specify how the controls were selected and it is not clear whether they undertook psychophysical olfactory testing to determine that their olfactory function was indeed normal. On the contrary, in this study we enrolled only subjects who scored normal at the extended version of the Sniffing test.

As for the clinical validity of the Brief-IT-QOD, patients with OD scored higher than normosmic subjects in both the parosmia and QoL subscales. Therefore, it is possible to speculate that Brief-IT-QOD may be a sensitive tool to discriminate olfactory-related QoL in patients with and without OD. Similar to our results, the original study [11] found a significantly higher QOD-P score in the hyposmic group (4.04 ± 3.13) than in the normosmic group (3.03 ± 2.84). On the other hand, Zou and colleagues [11] did not obtain significant differences in the QOL-QOD subscale between patients and controls. Conversely, in their validation of a shortened, 25-item version of the QOD, Simopoulos et al. [24] showed a significant difference in QOD-NS scores between patients and normosmic subjects, analogous to our results.
Furthermore, when analysing concurrent validity, we found positive correlations between the results of the extended version of the Sniffing test and Brief-IT-QOD subscales and between these subscale scores and I-SNOT-22. However, it should be noted that the two questionnaires do not measure the same constructs (QOD is specific for olfactory disturbances, while SNOT-22 investigates general sinonasal complaints but contains a question related to OD). Comparison with the available literature is again complex. To evaluate external validity, Leclercq et al. [23] used a visual analogue scale related to OD, while they did not perform a correlation analysis with SNOT-22. Conversely, neither Zou et al. [11] nor Chiesa-Estomba et al. [22] reported on external validity. Finally, Simopoulos et al. [24] did not assess the external validity of QOD-NS, but only that of QOD-positive statements.
The significant decrease recorded in Brief-IT-QOD scores after successful biologic therapy for recalcitrant CRSwNP suggests that Brief-IT-QOD is responsive to changes in the QoL of patients with OD. No previous report on responsiveness of QOD is available. However, the data reported herein (even if obtained in a small group of patients) support the clinical applicability of the Brief-IT-QOD in the monitoring of patients' outcomes.
Lastly, cut-off determination was carried out through ROC curve analysis, obtaining a QOD-P cut-off value of 3.5 and a QOL-QOD cut-off value of 1.5. No literature on this topic is available to make comparisons with the values we determined. However, the low sensitivity and specificity scores of the two subscales found in this study limit the use of the Brief-IT-QOD for screening purposes.

Study limitations

The present study has several limitations. First of all, the cross-cultural adaptation from English into Italian did not strictly follow international guidelines [12,25]. In fact, according to these, the cross-cultural adaptation of self-report measures is a five-stage process: translation (stage I), synthesis (stage II), back-translation (stage III), expert committee review (stage IV), and pretesting (stage V). In our study, pretesting was performed as a pilot study (step 3 of Phase 1) before back-translation and expert committee review; while this should be considered a limitation, we felt that patient input would be crucial to better define the items into Italian. This updated version was then subjected to expert review by the professionals involved (step 4 of Phase 1) and eventually underwent backward translation (step 5 of Phase 1). The process we adopted might have impacted the Brief-QOD final Italian version.
A second limitation lies in the fact that OD and not QoL reduction associated with OD was the criterion adopted to include both patients and healthy subjects in the study. This was due to the fact that a validated measure of OD-related QoL was not available in the Italian language. It is therefore theoretically possible that patients with OD did not present a reduction in OD-related QoL, and that, on the other hand, normosmic subjects might have presented a reduction in OD-related QoL, in turn. Besides, in the responsiveness analysis of the Brief-IT-QOD, it cannot be assumed that an improvement in olfactory function would have necessarily resulted in an improvement in QoL measures. However, the patients enrolled in this phase of the study improved their TDI scores at the Extended Smell Test by Sniffin' Sticks (Burghart Messtechnik GmbH, Germany). We assumed consequently that the improvement of olfactory abilities could be related to improvement of the Brief-IT-QOD.

Conclusions

The Brief-IT-QOD is a reliable and valid self-administered, symptom-specific outcome tool for OD in adult Italian patients. The application of a standardised OD-specific instrument in everyday clinical practice, such as the Brief-IT-QOD, as well as in epidemiological, efficacy, and outcome research is therefore recommended, as it can facilitate comparison of results of different studies.

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Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

FM, LL, RA, FrO: study conception and design; AC, AP, AA, DC, GM, FiO: material preparation and data collection; GP, FM: conducted the statistical analysis and interpretation of results. The first draft of the manuscript was written by AC, FM, GR, GP. All the Authors commented on previous versions of the manuscript and read and approved the final manuscript.

Ethical consideration

This study was approved by the Institutional Ethics Committee (Comitato Etico Indipendente IRCCS Multimedica) (Protocol n. 506.2021).

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

Written informed consent was obtained from each participant/patient for study participation and data publication.

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