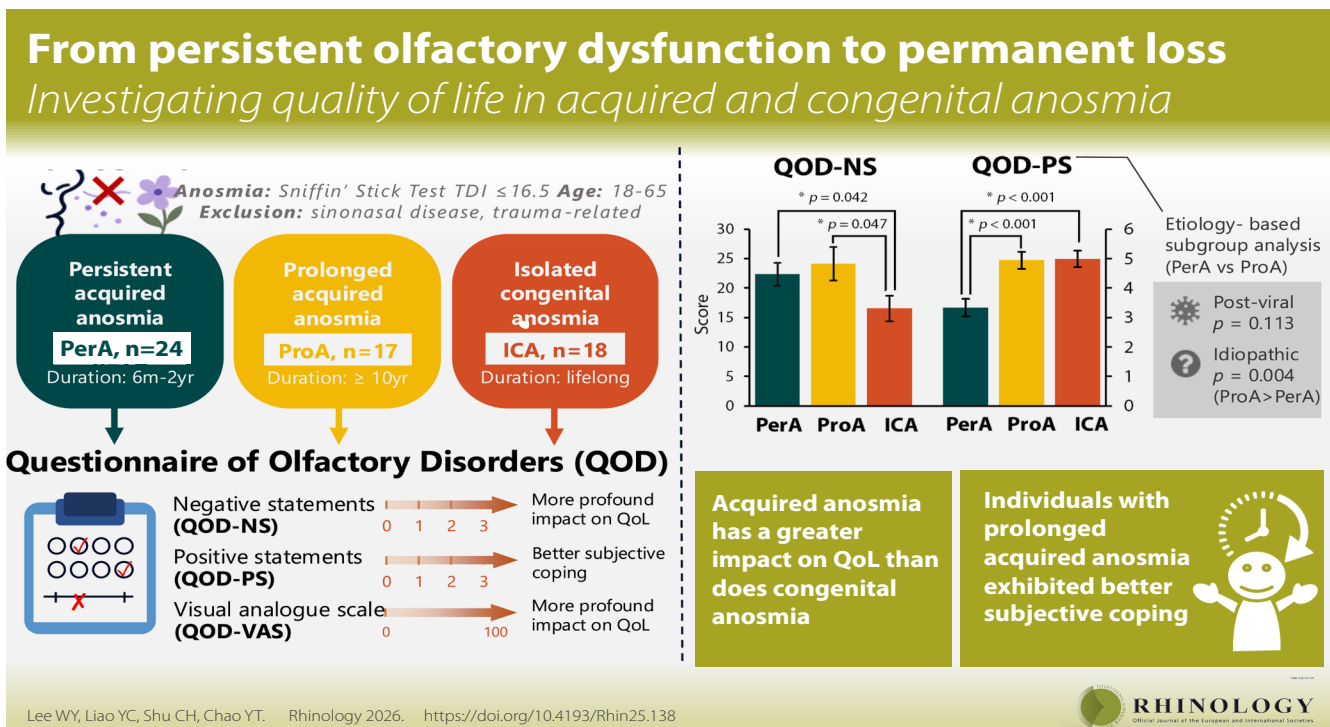


From persistent olfactory dysfunction to permanent loss:
investigating quality of life in acquired and congenital anosmia

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Abstract

Background: Growing awareness of permanent olfactory dysfunction has raised concerns about its impact on quality of life (QoL). This study examined the effect of permanent anosmia on QoL by comparing patients with acquired anosmia of varying durations, including cases persisting for over a decade and cases of isolated congenital anosmia (ICA).

Methodology: A total of 59 patients with post-viral or idiopathic anosmia who sought medical evaluation due to olfactory complaints completed the Questionnaire of Olfactory Disorders (QOD), which measured impairment, coping ability, and subjective disturbance. Patients were categorized into three groups: persistent acquired anosmia (PerA, duration 6 months–2 years), prolonged acquired anosmia (ProA, duration ≥10 years), and ICA to reflect distinct populations. Patients with intermediate or uncertain duration were excluded to avoid recall bias.

Results: Perceived impairment, as reflected by QOD-NS and work domain of QOD-VAS, was higher in the PerA and ProA groups than in the ICA group. No significant differences in QOD-NS and QOD-VAS were observed between PerA and ProA groups. The ProA group exhibited better coping ability, as indicated by higher QOD-PS scores, than did the PerA group, suggesting coping over time. Coping scores in the ProA and ICA groups were comparable, indicating long-term adjustment in anosmic individuals.

Conclusions: Acquired anosmia has a greater impact on QoL than does congenital anosmia. Individuals with prolonged acquired anosmia exhibited better subjective coping.

Key words: permanent anosmia, acquired anosmia, congenital anosmia, quality of life

Introduction

Olfaction is crucial for maintaining physical and mental well-being, fostering social connections, and enhancing overall quality of life (QoL) ⁽¹⁾. The loss or impairment of smell function brings numerous challenges, including a diminished enjoyment of food, increased risk of exposure to hazardous substances, and difficulties in maintaining personal hygiene, ultimately leading to social insecurity, emotional distress, and a decline in QoL ⁽²⁻⁴⁾.

Various standardized instruments have been developed to quantify the impact of olfactory impairments in terms of olfaction-related QoL ⁽⁵⁻⁸⁾. Surveys have also been conducted to evaluate the development of coping abilities for olfactory disorders ^(4,9). The Questionnaire of Olfactory Disorders (QOD) is widely used to assess the influences on QoL as well as the coping abilities of patients ⁽⁸⁾. These tools consistently demonstrate the negative effects of olfactory dysfunction on daily life, and QoL outcomes may vary depending on factors such as patient age, sex, or etiology ⁽¹⁰⁻¹³⁾. Despite this, previous research has failed to address one critical question: Do the negative effects on QoL persist or do they gradually subside?

Some researchers have reported that QoL gradually improves after olfactory loss as individuals adapt to their new circumstances ^(13,14). Other researchers have found that the duration of olfactory dysfunction does not significantly affect QoL ^(2,8,12,15). Nonetheless, as olfactory loss persists, the likelihood of recovery diminishes, often resulting in permanent anosmia ^(16,17). Recent concern about long COVID with persistent olfactory dysfunction has further emphasized the need to understand permanent olfactory loss and its impact on daily life, given the low recovery rates observed beyond six months ⁽¹⁸⁻²¹⁾. While prolonged olfactory dysfunction has received growing attention in recent years, its QoL impact remains less well understood in individuals with very long disease durations. In this study, we focused on individuals with post-viral or idiopathic anosmia and examined the impact of long-term anosmia in cases spanning a decade or more, approaching permanent olfactory loss.

To understand the effects of permanent olfactory dysfunction, it is essential to consider the effects of isolated congenital anosmia (ICA), a lifelong condition in which individuals are unable to perceive odour from birth. Many of these otherwise healthy patients exhibit daily-life functionality comparable to that of normosmic individuals; however, this does not imply that a lifelong absence of olfactory capacity has no impact on QoL ⁽²²⁾. Previous research on olfactory-related QoL has rarely compared long-term acquired anosmia with congenital anosmia, leaving a knowledge gap pertaining to these underexplored populations.

In the current study, we sought to clarify the impact of long-

term olfactory loss on QoL among patients with persistent acquired anosmia (duration six months to two years), prolonged acquired anosmia (duration of a decade or more), or ICA. This comparative approach provides a comprehensive understanding of QoL in individuals living with permanent anosmia, offering new insights into the challenges faced by these populations.

Materials and methods

Subjects

From a retrospective database review, we recruited patients with anosmia of varying etiologies and disease durations, who had completed the QOD survey ⁽¹²⁾. The etiology of olfactory loss was established through detailed history taking, physical examination, sinonasal endoscopy, and in ICA cases, brain magnetic resonance imaging (MRI) focusing on the olfactory bulb. A diagnosis of ICA was based on the following criteria: 1) medical history of never experiencing any odorous sensations since birth; 2) psychophysical testing confirming anosmia; 3) MRI findings demonstrating olfactory bulb aplasia, hypoplasia or flattened olfactory sulcus; and 4) exclusion of syndromic anosmia, such as Kallmann syndrome ⁽²³⁾.

Anosmia patients between 18 and 65 years of age were included in our study. Patients with sinonasal disease were excluded due to the possibility of symptom fluctuations or spontaneous recovery. Patients with trauma-induced anosmia were also excluded, as head trauma often leads to additional neurological or physical injuries that could confound QoL outcomes.

To investigate how the duration of anosmia influences QoL, patients with acquired anosmia were categorized into two distinct groups: persistent acquired anosmia (PerA; duration 6 months to 2 years) and prolonged acquired anosmia (ProA; duration ≥ 10 years). We deliberately set a clear and memorable cut-off at 10 years to define the ProA group, ensuring more accurate retrospective classification. In contrast, durations in the intermediate range (2–10 years) often fall into a “grey zone”, where onset recall is less precise and the degree of psychological adjustment is highly variable. To avoid transitional heterogeneity that could blur group differences and compromise interpretability, we excluded patients within this intermediate range. A group of ICA patients was also included as comparative subjects.

To determine the optimal sample size, power analysis was performed a priori using G*Power, version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany) ⁽²⁴⁾. The significance level was set at $\alpha=0.05$ and the desired power ($1-\beta$) was set at 0.80, assuming an effect size of $f=0.5$ ⁽²²⁾. Our analysis indicated that under these conditions, a total of 65 participants would be required to achieve the targeted power. All study procedures were conduc-

ted in strict adherence with the Declaration of Helsinki and were approved by the Institutional Review Board of our hospital (IRB No. 2017-07-012AC). All data were analysed anonymously and individual consent was waived.

Measuring olfactory function

Olfactory function was assessed using the Sniffin' Sticks test (Burghardt, Wedel, Germany), including threshold (T), discrimination (D), and identification (I) ⁽²⁵⁾. The threshold test involves identifying the lowest detectable odour concentration. The discrimination test assesses the ability to distinguish one different odour from two identical odours. The identification test assesses the ability to match a given odour to its corresponding source in a list of four items. Some of the descriptors in the identification test were modified from the original version of the Sniffin's Sticks test in accordance with cultural norms, based on a previously validated Taiwanese version ^(26,27). T score ranged from 1 to 16, while D and I scores each ranged from 0 to 16. The three test scores were summed, yielding the TDI score, which was used to categorize cases as normosmia, hyposmia, or anosmia. In this study, anosmia was defined by a TDI score ≤ 16.5 ⁽²⁸⁻³¹⁾.

To examine the effect of residual olfactory function in acquired anosmic patients, we first defined a complete anosmia group, which included individuals with a threshold score of 1, as well as those with higher threshold scores but TDI values falling within the lowest 10th percentile of the cohort. The remaining patients with residual olfactory function were classified into the non-complete anosmia group.

Questionnaire of Olfactory Disorder

The Questionnaire of Olfactory Disorder comprises 19 statements, including 17 negative statements (QOD-NS) and 2 positive statements (QOD-PS) ^(8,12). Negative statements indicate the negative effects of olfactory impairment, such as "Because of the changes in my sense of smell, I go to restaurants less often than I used to" and "Because of the changes in my sense of smell, I try harder to relax". Positive statements reflect the ability to cope with olfactory loss such as "I can imagine adjusting to my difficulties with smelling".

Participants express their agreement with each statement by selecting one of the following options: "I agree," "I partly agree," "I partly disagree," or "I disagree". Each item was scored on a scale of 0 to 3 points, where a higher score for negative statements indicates a more profound impact on daily life, while a higher score for positive statements indicates a greater ability to cope with olfactory loss.

The questionnaire also includes a visual analogue scale (QOD-VAS), where patients mark a point on a line representing a

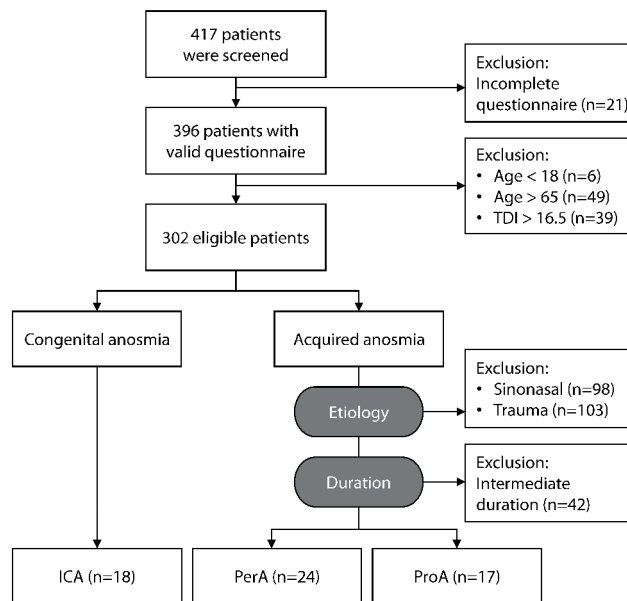


Figure 1. Flowchart illustrating the patient selection process. An initial screening of 417 patients yielded 396 valid questionnaires. After applying exclusion criteria, the remaining 59 patients were categorized into three groups: PerA (persistent acquired anosmia, symptoms lasting 6 months–2 years, n=24), ProA (prolonged acquired anosmia, symptoms lasting ≥ 10 years, n=17), and ICA (isolated congenital anosmia, n=18).

spectrum of subjective disturbance between "the least" (score 0) and "the most" (score 100) profound effects. The VAS items were designed to assess the following: 1) the extent of disturbance, 2) the frequency of awareness of olfactory issues, 3) the influence on work, 4) the influence on leisure activities, and 5) the influence on private life.

All participants were assessed at their initial visit, prior to receiving any treatment such as medication or olfactory training. Patients completed the questionnaire independently, without interviewer administration or remote submission. Each response sheet was immediately reviewed by trained staff to confirm completeness and accuracy.

Statistical analysis

Statistical analysis was conducted using JASP (Version 0.18.3, 2024) (<https://jasp-stats.org/>). Categorical variables were analysed using the Chi-square test or Fisher's exact test. Continuous variables were compared using the Mann-Whitney U test or analysis of covariance (ANCOVA), followed by Dunn's post hoc test for pairwise comparisons, with age included as a covariate. Correlations were evaluated using Spearman's coefficient (r). In addition, a multivariable linear regression analysis was performed with age and anosmia duration group as independent variables and QOD scores as dependent variables. Statistical significance was set at $p < 0.05$ with a 95% confidence level.

Table 1. Baseline characteristics of study participants.

	PerA (n=24)	ProA (n=17)	ICA (n=18)	F	χ^2	p-value
Age	45.63±10.25	51.88±8.33	38.28±13.42	6.909		0.002*
Male	7 (29.2%)	7 (41.2%)	12 (66.7%)		5.949	0.051
TDI score	11.54±2.98	10.34±3.48	10.46±3.12	0.929		0.401
Threshold	1.13±0.27	1.10±0.18	1.29±0.54	1.557		0.220
Discrimination	5.71±1.46	5.18±2.30	5.22±2.60	0.417		0.661
Identification	4.58±2.21	4.06±1.85	3.94±1.73	0.638		0.532
Etiology					0.161	0.688
Viral infection	7 (29.2%)	4 (23.5%)	-			
Idiopathic	17 (70.8%)	13 (76.5%)	-			

Data are presented as mean ± SD. *Indicates statistical significance in one-way ANOVA test. Abbreviations: PerA: Persistent acquired anosmia; ProA: Prolonged acquired anosmia; ICA: Isolated congenital anosmia.

Results

Patient characteristics

A total of 59 individuals meeting our inclusion and exclusion criteria were enrolled, including 24 patients in the PerA group, 17 in the ProA group, and 18 in the ICA group (Table 1). Figure 1 presents a schematic illustration of the patient selection process. No differences of statistical significance were observed in the gender distribution or TDI scores among the three groups. The average age was significantly lower in the ICA group (38.28±13.42 years) than in the ProA group (51.88±8.33 years; $p=0.001$). The mean duration of olfactory loss was 0.96 years (range 0.5-2) in the PerA group and 21.12 years (range 10-50) in the ProA group. No significant differences in the underlying etiology (post-viral vs. idiopathic) were detected between the PerA and ProA groups.

Statements scores (QOD-PS, QOD-NS)

Figure 2 and Table S1 present the results of QOD-NS and QOD-PS. After adjusting for age, the ANCOVA results revealed significant differences in QOD-NS ($p=0.040$), and QOD-PS ($p<0.001$) among the three groups. Post hoc analysis revealed that QOD-NS scores were significantly higher in the PerA group compared to the ICA group ($p=0.042$) and in the ProA group compared to the ICA group ($p=0.047$). No significant differences were detected between the PerA and ProA groups. For the QOD-PS scores, both the ProA and ICA groups had significantly higher scores than the PerA group ($p<0.001$ for both comparisons).

Visual Analogue Scale (QOD-VAS)

QOD-VAS scores were higher among patients with acquired anosmia (PerA and ProA) compared to those with ICA, consistent with the trend observed in QOD-NS scores (Figure 3). ANCOVA revealed significant differences among the three groups in awareness ($p=0.045$), work ($p=0.032$), leisure ($p=0.012$) and private

($p=0.025$) domains. A trend toward significance was observed in the disturbance domain ($p=0.054$) (Table S1). In the Leisure domain, the ProA group demonstrated significantly higher scores than the ICA group ($p=0.028$). In the Work domain, both the PerA and ProA groups exhibited significantly higher scores than the ICA group ($p=0.047$ and $p=0.025$, respectively).

Subgroup, correlation and regression analyses in acquired anosmia

When stratified by anosmia severity, Mann-Whitney U tests revealed no significant difference between complete anosmia group ($n=29$) and non-complete anosmia group ($n=12$) in QOD-NS, QOD-PS, or QOD-VAS domains (Table S2).

In etiology-based subgroup analyses, no significant group differences in QOD-NS, QOD-PS, or QOD-VAS scores were observed between the PerA group ($n=7$) and the ProA group ($n=4$) in post-viral anosmia patients. Among idiopathic anosmia patients, QOD-PS scores were significantly higher in the ProA group ($n=13$) compared to the PerA group ($n=17$) ($U=42.5$, $p=0.004$). No other domains showed significant group differences (Table S3).

In Spearman correlation analyses of the acquired anosmia patients, both age ($\rho=0.328$, $p=0.036$) and duration ($\rho=0.462$, $p=0.002$) were positively correlated with QOD-PS, but neither was associated with QOD-NS or QOD-VAS domains (Table S4).

Multivariable linear regression demonstrated that longer duration (ProA group) was independently associated with higher QOD-PS scores ($p=0.002$), whereas age was not significantly associated ($p=0.580$). No significant associations were observed for QOD-NS or any QOD-VAS domains (Table S5).

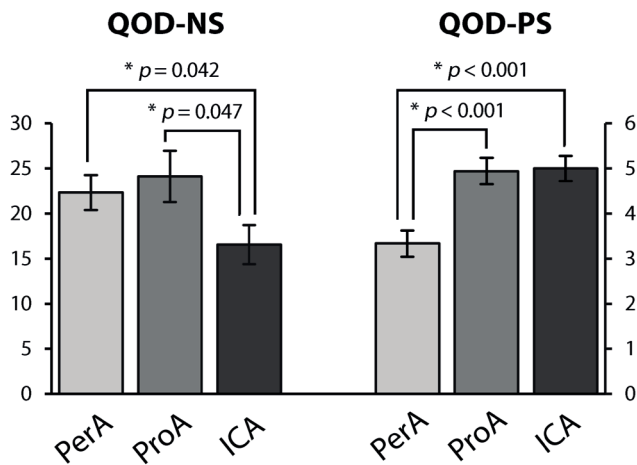


Figure 2. QOD-NS and QOD-PS scores in the PerA, ProA, and ICA groups. * Indicates statistical significance in post-hoc analysis. QOD-NS: Questionnaire of Olfactory Disorders-Negative Statements; QOD-S: Questionnaire of Olfactory Disorders-Positive Statements; PerA: Persistent acquired anosmia; ProA: Prolonged acquired anosmia; ICA: Isolated congenital anosmia.

Discussion

This study examined the impact of persistent and prolonged anosmia on olfaction-related QoL, focusing on post-viral and idiopathic anosmia as well as ICA. Comparisons between the PerA and ProA groups revealed that among patients with acquired anosmia, impairment levels in QOD-NS and QOD-VAS (across several domains) were unaffected by the duration of olfactory loss. Overall, ProA patients demonstrated better coping abilities, as reflected by their higher QOD-PS scores. Moreover, ICA patients experienced less QoL compromise compared to those with acquired anosmia.

No significant differences in QOD-NS and QOD-VAS scores were observed between the PerA and ProA groups, and no significant correlations were found between duration and either QOD-NS or QOD-VAS, suggesting that olfaction-related QoL is largely unaffected by the duration of olfactory loss. Our review of the literature revealed inconsistent findings pertaining to the relationship between disease duration and QoL (Table 2)^(2,8,12-15). These discrepancies may stem from several methodological differences. First, heterogeneity in patient populations may have influenced the outcomes. For example, Neuland et al. focused predominantly on idiopathic cases, whereas Shu et al. included a large portion of trauma-related and sinonasal disease-related cases^(12,15). Second, the analysis of duration varied, with some considered it as a continuous variable, while others used relatively short categorical cutoffs such as 30-day thresholds^(12,14). Third, broader instruments such as the SF-36 were used as outcome measure in some literature, which may capture

domains beyond olfaction⁽¹⁵⁾. In contrast, we focused specifically on idiopathic or post-viral anosmia. We excluded patients with sinonasal disease due to fluctuating olfactory function, as well as those with trauma-induced anosmia, as their QoL could be affected by additional neurological or physical impairments. By including patients with nearly lifelong anosmia (duration ≥ 10 years), this study provides a unique perspective on QoL over extended periods.

Beyond its clinical significance, the 10-year threshold may also function as a “temporal landmark” in cognitive neuroscience, providing a salient and memorable benchmark for patients to determine whether their anosmia has persisted for at least a decade⁽³²⁾. As a decade marker, it helps to establish distinct temporal categories and to maximize contrast in QoL differences between recent and long-standing anosmia. Developmental insights from ICA further support the 10-year threshold, as awareness of the deficit typically emerges around age ten, when olfactory cues become socially and environmentally relevant⁽³³⁾. By extension, acquired anosmia lasting over a decade not only indicates chronicity but also reflects psychological integration. Future studies may consider a more granular classification to further validate these findings.

Patients with ICA exhibited lower QOD-NS than did those with acquired anosmia. Despite being unable to smell since birth, they appear to function in daily life nearly as well as healthy individuals⁽²²⁾. In contrast, patients with acquired anosmia deal with frustration as they lose touch with their perceptions of the world previously shaped by olfactory experiences. A similar phenomenon has been described in ophthalmology, where patients with acquired blindness reported a poorer vision-related QoL compared to congenital cases⁽³⁴⁾. Taken together, these findings suggest that sensory loss has a more profound impact on QoL when it disrupts pre-existing sensory functions and habitual activities.

In this study, the QOD-PS scores of ProA patients were higher than those of PerA patients, indicating better subjective coping in patients with prolonged anosmia. When stratified by etiology, this difference remained significant in the idiopathic subgroup ($U=42.5$, $p=0.004$). In post-viral patients, a similar trend was observed but did not reach statistical significance. The difference may be partly explained by variation in symptom onset. Whereas idiopathic anosmia may develop insidiously, post-viral anosmia typically follows an abrupt smell loss after infection⁽³⁵⁾. The sudden nature of onset may limit psychological preparation, making it more difficult for individuals to adjust to the disruption in daily life⁽³⁶⁾.

Correlation analysis showed that anosmia duration was posi-

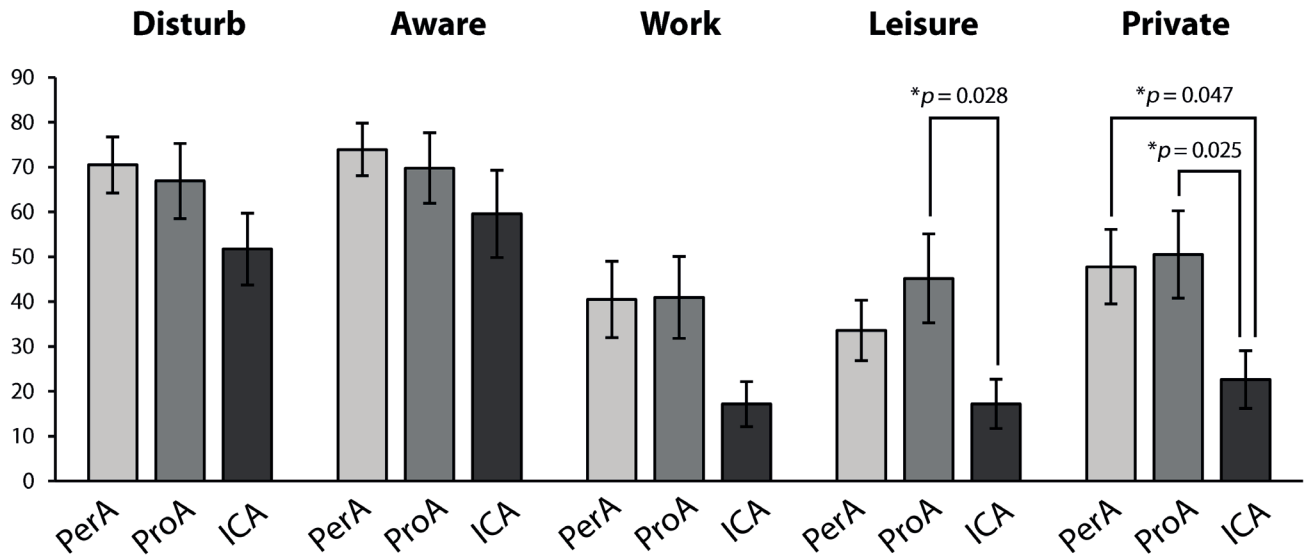


Figure 3. QOD-VAS scores in the PerA, ProA, and ICA groups across five domains: disturbance, awareness, work, leisure, and private life. * Indicates statistical significance in post-hoc analysis. QOD-NS: Questionnaire of Olfactory Disorders-Negative Statements; QOD-PS: Questionnaire of Olfactory Disorders-Positive Statements; PerA: Persistent acquired anosmia; ProA: Prolonged acquired anosmia; ICA: Isolated congenital anosmia

vely associated with QOD-PS scores in patients with acquired anosmia ($p=0.462$, $p=0.002$). This association suggests that coping abilities may improve with longer disease duration, potentially reflecting emotional adjustment over time. One possible psychological mechanism is placing less emphasis on the sense of smell⁽³⁷⁾. In addition, qualitative study have described a transition from initial isolation to self-identification as ‘anosmic’, eventually leading to the development of resilience⁽³⁸⁾.

While our study assessed coping capacity through QOD-PS scores, it did not evaluate the use or effects of specific adapting strategies or interventions, such as olfactory training or multisensory therapy. Olfactory training, involving repeated exposure to a set of distinct odours over months, has been shown to improve QoL in individuals with olfactory dysfunction⁽³⁹⁻⁴¹⁾. Distressing consequences of olfactory loss such as reduced enjoyment of food can also be addressed by engaging other sensory modalities. Individuals can create a richer eating experience by emphasizing texture, temperature, and tactility in conjunction with trigeminal nerve stimulation. A notable example is a five-week cooking school program designed for individuals with olfactory loss⁽⁴²⁾. This intervention provided participants with seasoning kits and modified recipes tailored based on participant feedback. Participants showed significant improvements in cooking confidence, enjoyment of food, and overall QoL, underscoring the potential of multisensory strategies for long-term adaptation.

Previous studies have shown that worse olfactory function is associated with greater impact on QoL^(8,12,15). However, these

findings were largely based on broader TDI ranges. In our analysis focusing on patients with acquired anosmia, no significant differences in QOD-NS, QOD-PS, or any QOD-VAS domains were observed between those with complete anosmia and those with partial residual function. These findings suggest that, once the diagnostic threshold for anosmia is met, residual olfactory function may not substantially influence QoL, as minimal olfactory input is generally insufficient for daily function such as food enjoyment. Future studies with larger samples and more targeted outcome measures may help clarify whether subtle residual olfaction has clinical relevance.

In this study, the ICA group was significantly younger than the ProA group. Previous research has shown that younger individuals with acquired olfactory dysfunction tend to report higher QOD-NS scores (more severe impact), while older individuals tend to report higher QOD-PS scores (better coping abilities)⁽¹²⁾. Our data partially supported these findings, showing a positive correlation between age and QOD-PS, but no significant association between age and QOD-NS. To account for possible confounding effects, we performed ANCOVA with age adjustment, which confirmed significant between-group differences in QOD-NS and QOD-PS. Nonetheless, this potential age effect on QoL outcomes is unlikely to have biased our conclusion that ICA patients (the youngest group in our study) exhibited better QoL outcomes than those with acquired anosmia. Moreover, our primary aim was to compare the impact of symptom duration on patients within the PerA and ProA groups. The two groups did not differ significantly in age, and multivariable linear regression further demonstrated that longer duration (ProA group)

Table 2. Review of the literature addressing the impact of olfactory dysfunction duration on quality-of-life impairment.

Study (year)	Patient number	Population (n, %)	Etiology (n, %)	Duration of olfactory dysfunction	Outcome measure	Influence of olfactory dysfunction duration
Temmel AF (2002)	278	Hyposmia (127, 45.7%), anosmia (151, 54.3%)	Post-URI (102, 36%), SND ¹ (60, 21%), idiopathic (51, 18%), trauma (47, 17%), congenital (9, 3%), others (9, 3%)	Group A: < 24 Group B: 24-48 Group C: > 48 (months)	Complaint score of self-reporting questionnaire	No significant difference between groups in terms of complaint scores (Kruskal-Wallis test)
Frasnelli J (2005)	205	Hyposmia (103, 50%), functional anosmia (81, 40%), normosmia (21, 10%)	N/A	Parosmia group: 23.3 Non-parosmia group: 56.5 (months, mean)	QOD	No significant correlation between olfactory dysfunction duration and QOD results (Pearson correlation, $r < 0.078$, $p > 0.28$)
Shu CH (2011)	413	N/A	Trauma (125, 30.3%), SND (103, 24.9%), idiopathic (95, 23%), post-viral (64, 15.5%)	N/A	QOD	No significant correlation between olfactory dysfunction duration and QOD-NS scores (Pearson correlation, $r = -0.014$, $p = 0.796$)
Neuland C (2011)	280	Severe hyposmia ² (75, 26.8%), anosmia (205, 73.2%)	Idiopathic (221, 78.9%), chronic rhinosinusitis (31, 11.1%), post-infectious (15, 5.4%), trauma (13, 4.6%)	3 (years, median)	QOD, SF-36	No significant difference between groups in terms of QOD or SF-36 results ³ (Mann-Whitney U-test, all $p > 0.05$)
Zou LQ (2021)	733	Functional anosmia (356, 48.57%), hyposmia (327, 44.61%), normosmia (50, 6.82%)	Post-infectious (243, 33.2%), idiopathic (242, 33.0%), SND (122, 16.6%), trauma (108, 14.7%), congenital (11, 1.5%), Neurodegenerative (7, 1.0%)	3.51 ± 6.57 (years, mean ± SD)	QOD	Negative correlation between OD duration and QOD-QOL score (Pearson correlation, $r = -0.119$, $p = 0.001$, $n = 713$), QOD-VAS score ($r = -0.101$, $p = 0.037$, $n = 429$), or QOD-P score ($r = -0.187$, $p < 0.001$, $n = 713$)
Liu DT (2022)	149	Hyposmia (16, 27.6%), anosmia (42, 72.4%)	Post-viral (149, 100%)	Pre-pandemic group: ≥ 30 New-onset COVID-19 group: < 30 Persistent COVID-19 group: ≥ 30 (days)	QOD	Lower QOD-NS scores in the pre-pandemic group compared with the new-onset COVID-19 group. ($p = 0.0098$, Tukey's post-hoc comparison tests)

¹ Abbreviation: sinonasal disease; ² TDI sum score < 20 points, symptom duration > 6 months; ³ The results of patients with symptoms lasting longer than the median duration of dysfunction of 3 years did not differ from those of patients with dysfunction lasting less than 3 years.

remained significantly associated with higher QOD-PS scores after controlling for age, confirming that the observed effect of duration was independent of age.

Our study was subject to several limitations. First, the relatively small sample size may have limited statistical power, making it difficult to detect subtle between-group differences. Future multicenter studies or larger cohorts are needed to improve generalizability. Second, the retrospective design introduced inherent limitations in data collection and biases. For example, self-reported disease duration is prone to recall bias, particularly in idiopathic cases with gradual or unrecognized onset. In prolonged cases, a high cutoff of ten years was applied to define ProA group, aiming to minimize recall bias by including only individuals who could confidently report long-standing anosmia. Additionally, we employed categorical grouping rather than continuous duration analysis for primary outcomes to reduce the influence of potential reporting inaccuracies. Third, selection

bias may have been introduced, as tertiary care centers typically receive individuals with more severe or distressing symptoms. Consequently, those with milder conditions who did not seek medical care or follow-up may have been underrepresented. Indeed, many individuals with olfactory dysfunction remain unaware of their impairment and report well-being comparable to normosmic individuals, making them less likely to be included in clinical samples⁽⁴³⁾. Fourth, potentially relevant variables—such as socioeconomic status, education level, and intrinsic psychological characteristics—were unavailable in the retrospective dataset, limiting our ability to examine their influence on QoL outcomes. Additionally, dependence solely on the QOD limited assessment of nuanced emotional and behavioral adaptations. Incorporating qualitative data or standardized psychological measures would supplement the interpretation of QOD scores in future studies. While the culturally adapted Sniffin' Sticks identification test may introduce slight variability compared with international studies, its use in diagnostic classification (rather

than outcome measurement) and prior validation in Taiwanese populations likely minimized its impact on our results. Lastly, the dataset was collected prior to the COVID-19 pandemic. Since then, public awareness of olfactory dysfunction has increased significantly, potentially altering health-seeking behavior and patients' subjective interpretation of symptoms. Lower awareness in earlier years potentially exacerbated feelings of isolation, influencing how QoL was perceived and reported. Despite these limitations, our findings offer valuable insights into the long-term psychosocial experience of individuals living with anosmia. Future prospective studies with larger and more diverse samples, longitudinal follow-up, and broader outcome measures will be essential to confirm and extend our observations on the impact of permanent olfactory dysfunction on QoL.

Conclusion

Growing public awareness of permanent olfactory dysfunction, especially in the context of long COVID, has raised concern about its long-term impact on QoL. Our findings suggest that QoL impairment is more pronounced in individuals with post-viral or idiopathic acquired anosmia before the COVID-19 pandemic than in those with congenital anosmia. Notably, patients with prolonged acquired anosmia reported a greater sense of

coping compared to those with more recent onset.

Author contributions

Study idea and design: WYL, YTC; data collection: YCL, CHS, YTC; data analysis: WYL, YTC; manuscript writing: WYL, YTC; final approval: all authors.

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Conflict of interest

The authors claim that there are no conflicts of interest.

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SUPPLEMENTARY MATERIAL

Table S1. Questionnaire scores assessing impact of olfactory dysfunction duration on the quality of life impact in patients with PerA, ProA, and ICA.

	PerA (n=24)	ProA (n=17)	ICA (n=18)	F	p-value
QOD-NS	22.33±9.49	24.12±11.71	16.56±9.21	3.426	0.040*
QOD-PS	3.33±1.44	4.94±1.20	5.00±1.19	12.625	<0.001*
QOD-VAS					
Disturb	70.50±30.56	66.88±34.68	51.72±34.00	3.089	0.054
Aware	73.92±28.81	69.76±32.39	59.56±41.32	3.275	0.045*
Work	40.50±41.70	40.94±37.66	17.17±21.22	3.673	0.032*
Leisure	33.58±32.94	45.18±40.88	17.22±23.16	4.844	0.012*
Private	47.79±40.84	50.53±40.16	22.61±27.31	3.952	0.025*

Data are presented as mean ± SD. * Indicates statistical significance in ANCOVA test. Abbreviations: PerA: Persistent acquired anosmia; ProA: Prolonged acquired anosmia; ICA: Isolated congenital anosmia; QOD-NS: Questionnaire of Olfactory Disorder-Negative statements; QOD-PS: Questionnaire of Olfactory Disorder-Positive Statements; QOD-VAS: Questionnaire of Olfactory Disorder-Visual analogue scale.

Table S2. Comparison of QOD scores between complete and non-complete anosmia groups among acquired anosmia patients.

	Complete anosmia group (n=29)	Non-complete anosmia group (n=12)	U	p-value
QOD-NS	22.83±11.60	23.67±6.88	155.5	0.605
QOD-PS	3.93±1.51	4.17±1.70	148.5	0.460
QOD-VAS				
Disturb	67.48±33.49	72.67±28.96	170.0	0.920
Aware	72.45±31.21	71.58±28.23	195.0	0.554
Work	45.14±42.34	29.92±30.92	206.0	0.362
Leisure	40.83±37.94	32.50±33.22	193.5	0.583
Private	47.83±41.63	51.58±37.64	180.5	0.863

Data are presented as mean ± SD. *Mann-Whitney U test. Abbreviations: QOD-NS: Questionnaire of Olfactory Disorder-Negative statements; QOD-PS: Questionnaire of Olfactory Disorder-Positive Statements; QOD-VAS: Questionnaire of Olfactory Disorder-Visual analogue scale.

Table S3. Subgroup analysis of QOD scores between PerA and ProA groups stratified by etiology

		PerA	ProA	U	p-value
QOD-NS	Post-viral	25.57±9.78	28.25±12.87	12.5	0.850
	Idiopathic	21.00±9.33	22.85±11.58	104.5	0.818
QOD-PS	Post-viral	2.57±1.51	4.25±1.26	5.5	0.113
	Idiopathic	3.65±1.32	5.15±1.14	42.5	0.004*
QOD-VAS					
Disturb	Post-viral	83.00±16.23	68.00±45.93	15.0	0.924
	Idiopathic	65.35±33.88	66.54±32.79	106.5	0.883
Aware	Post-viral	79.86±17.55	64.25±45.18	16.0	0.775
	Idiopathic	71.47±32.50	71.46±29.59	116.5	0.817
Work	Post-viral	57.43±43.34	53.00±50.43	13.5	1.000
	Idiopathic	33.53±40.23	37.23±34.52	96.5	0.569
Leisure	Post-viral	49.14±37.55	65.75±44.78	10.0	0.506
	Idiopathic	27.18±29.70	38.85±39.27	85.5	0.301
Private	Post-viral	62.86±35.47	65.75±45.84	13.0	0.924
	Idiopathic	41.59±42.26	45.85±39.04	94.5	0.515

Data are presented as mean ± SD. * Indicates statistical significance in Mann-Whitney U test. ** Sample sizes: Post-viral anosmia: PerA (n = 7), ProA (n = 4); Idiopathic: PerA (n = 17), ProA (n = 13). Abbreviations: PerA: Persistent acquired anosmia; ProA: Prolonged acquired anosmia; QOD-NS: Questionnaire of Olfactory Disorder-Negative statements; QOD-PS: Questionnaire of Olfactory Disorder-Positive Statements; QOD-VAS: Questionnaire of Olfactory Disorder-Visual analogue scale.

Table S4. Spearman correlation between age, duration of anosmia, and QOD scores in patients with acquired anosmia (Spearman's correlation coefficients (ρ), corresponding p-values).

	Age (ρ , p)	Duration (ρ , p)
QOD-NS	-0.170, 0.288	-0.003, 0.986
QOD-PS	0.328, 0.036*	0.462, 0.002*
QOD-VAS		
Disturb	-0.040, 0.804	0.057, 0.723
Aware	-0.070, 0.663	-0.068, 0.674
Work	-0.144, 0.368	0.024, 0.884
Leisure	-0.269, 0.089	0.097, 0.546
Private	-0.156, 0.331	0.025, 0.877

* Indicates statistical significance in Spearman correlation. Abbreviations: QOD-NS: Questionnaire of Olfactory Disorder-Negative statements; QOD-PS: Questionnaire of Olfactory Disorder-Positive Statements; QOD-VAS: Questionnaire of Olfactory Disorder-Visual analogue scale.

Table S5. Association of QOD scores with age and anosmia duration group (reference: PerA group) in patients with acquired anosmia.

	Covariates	β (95% CI)	p-value
QOD-NS	Age	-0.123 (-0.487 – 0.230)	0.473
	Duration group	0.125 (-4.528 – 9.703)	0.466
QOD-PS	Age	0.081 (-0.033 – 0.059)	0.580
	Duration group	0.492 (0.612 – 2.444)	0.002*
QOD-VAS			
Disturb	Age	-0.136 (-1.547 – 0.666)	0.425
	Duration group	-0.013 (-22.811 – 21.092)	0.937
Aware	Age	-0.211 (-1.667 – 0.385)	0.214
	Duration group	-0.002 (-20.499 – 20.214)	0.989
Work	Age	-0.119 (-1.852 – 0.899)	0.488
	Duration group	0.043 (-23.868 – 30.710)	0.801
Leisure	Age	-0.301 (-2.311 – 0.096)	0.070
	Duration group	0.254 (-5.356 – 42.398)	0.125
Private	Age	-0.207 (-2.212 – 0.535)	0.224
	Duration group	0.099 (-19.262 – 35.232)	0.557

* Indicates statistical significance in multivariable linear regression. Abbreviations: PerA: Persistent acquired anosmia; QOD-NS: Questionnaire of Olfactory Disorder-Negative statements; QOD-PS: Questionnaire of Olfactory Disorder-Positive Statements; QOD-VAS: Questionnaire of Olfactory Disorder-Visual analogue scale; β : standardized regression coefficient; CI: confidence interval.