Rhinology Online
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ORIGINAL CONTRIBUTION

OPEN ACCESS

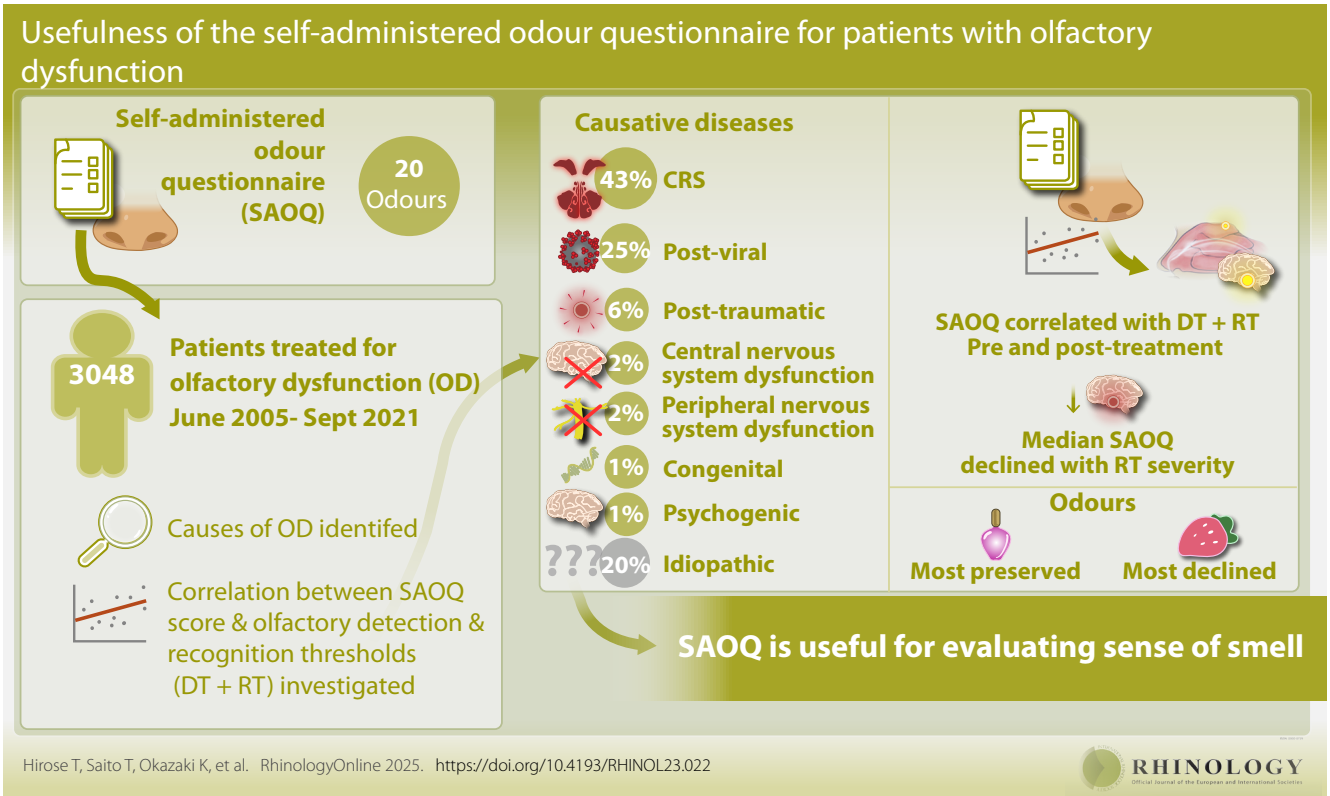
Usefulness of the self-administered odour questionnaire for patients with olfactory dysfunction*

Tomoki Hirose, Takahiro Saito, Ken Okazaki, Katsuya Fushimi, Kenzo Tsuzuki

Department of Otorhinolaryngology - Head and Neck Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan

Rhinology Online, Vol 8: 1 - 8, 2025
http://doi.org/10.4193/RHINOL/23.022

***Received for publication:**
August 17, 2023
Accepted: January 13, 2025
Published: February 1, 2025



Abstract

Background: The self-administered odour questionnaire (SAOQ), consisting of 20 odours familiar to Japanese people, is proposed as a scoring system for the quantitative evaluation of sense of smell. We examined the correlations between the SAOQ and the standard olfactory test covered by insurance in Japan and evaluated the usefulness of the SAOQ in patients with olfactory dysfunction (OD).

Methodology: Data from 3048 patients undergoing treatment for OD between June 2005 and September 2021 were retrospectively analysed. The causative diseases of OD were identified. Correlations between the SAOQ score and olfactory detection and recognition thresholds (DT and RT) were investigated using olfaction tests. The characteristics of each itemised odour of the SAOQ for each causative disease were analysed.

Results: Causative diseases of OD were: chronic rhinosinusitis (43%), post-viral (25%), post-traumatic (6%), central nervous system dysfunction (2%), peripheral nervous system dysfunction (2%), congenital (1%), psychogenic (1%), or idiopathic (20%). The SAOQ

score correlated with DT and RT in both the pre- and post-treatment stages. The median SAOQ scores significantly declined with RT severity. Analysis of the itemised odour scores of the SAOQ showed that 'strawberry' was the most declined-odour, while 'perfume' was the most preserved-odour.
Conclusions: The SAOQ is a useful scoring interview system for evaluating sense of smell.

Key words: odour, olfaction, questionnaire, score, smell

Introduction

Olfactory dysfunction (OD) is associated with life-threatening hazards due to delayed avoidance of danger [1], mental health damage such as depression and anxiety, limited social isolation and behaviour [2-4], physical damage such as frailty [5], decreased performance and productivity, and reduced quality of life [2-4]. OD is also one of the prodromal symptoms of neurodegenerative diseases, such as Alzheimer's disease [6-8] and Parkinsonism [9-11]. Therefore, early detection of OD is important. The population of patients with OD is not insignificant [12], and the prevalence of anosmia is approximately 5% in the general population [2]. The importance of olfactory evaluation has been emphasised. However, olfactory tests are still not widespread in Japan because of methodologically complicated problems. In Japan, the standard olfactory test using a T&T olfactometer and intravenous olfactometry are covered by insurance as olfaction tests in OD. Both tests require manpower and cost, and deodorisation equipment is required for the standard olfactory test using a T&T olfactometer. A 2007 UK-based survey reported that although 97% of otorhinolaryngologists managed OD, 55% did not formally test for chemosensory impairment, and of those who did, only 12% did so routinely [13]. Thus, as one of the indicators for the detection of OD, the self-administered odour questionnaire (SAOQ), which consists of 20 odours familiar to the Japanese population, was initially proposed by the Japan Rhinologic Society in 2003 [14]. The SAOQ is very simple, with patients answering a single questionnaire form for 20 odours. It also requires no manpower or cost and takes only 1-2 minutes to complete. The purpose of this study was to clarify the usefulness of the SAOQ and the characteristics of each SAOQ odour in patients with OD and to discuss its contribution to the management of OD in clinical practice.

Methods

Patients

Between June 2005 and September 2021, 3048 patients (1278 men and 1770 women; median age, 59 years; age range 4-95 years) with OD who were treated at our hospital and completed the SAOQ were enrolled in this study. Patients who answered 'not recently smelled or never smelled' for more than 11 odours on the SAOQ (n = 94) were excluded from this study.
This study used a case series design and was approved by the ethics committee of Hyogo Medical University (approval number 1512). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Diagnosis of causative diseases

The causes of OD were chronic rhinosinusitis (CRS), post-viral (PV), post-traumatic (PT), central nervous system dysfunction (CNS), peripheral nervous system dysfunction (PNS), congenital, psychogenic, and idiopathic [15]. CRS was diagnosed in patients with upper respiratory symptoms, and imaging (computed tomography, CT; magnetic resonance imaging, MRI) delineated the occupied lesions in the paranasal sinuses according to the previous position paper [16]. PV OD was diagnosed when there was a history of upper respiratory tract viral infection and smell loss persisted after the resolution of the upper respiratory symptoms, and there were no obvious lesions in the sinonasal area on nasal endoscopy and imaging (CT or MRI). PT OD was diagnosed when OD occurred in association with obvious head or facial trauma. CNS OD was diagnosed in patients with neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, diagnosed by a neurologist, in patients with intracranial lesions, and in patients who underwent neurosurgical procedures. Congenital OD was diagnosed by interviewing patients and their families and/or by the presence of deficiency, deficit, or hypoplasia of the olfactory bulb on MRI. PNS OD was defined as the presence of diseases affecting the PNS, such as anaemia, zinc deficiency, diabetes mellitus, herpes simplex, and herpes zoster. When no cause of OD could be identified, the cause of OD was diagnosed as idiopathic.

Treatments

Surgery and conservative treatments (low-dose macrolides, topical and systemic steroid treatments) were performed for CRS. For other causative diseases, except psychogenic and congenital OD, conservative treatments (olfactory training [17], vitamin B12, Chinese herbal medicine called Tokisyakuyakusan [18]) were performed.

Olfactory evaluation

Self-administered odour questionnaire (SAOQ)

The SAOQ was developed by the Japan Rhinologic Society in 2003. We administered the SAOQ to patients with OD at the first outcome visit in January 2005. The questionnaire consists

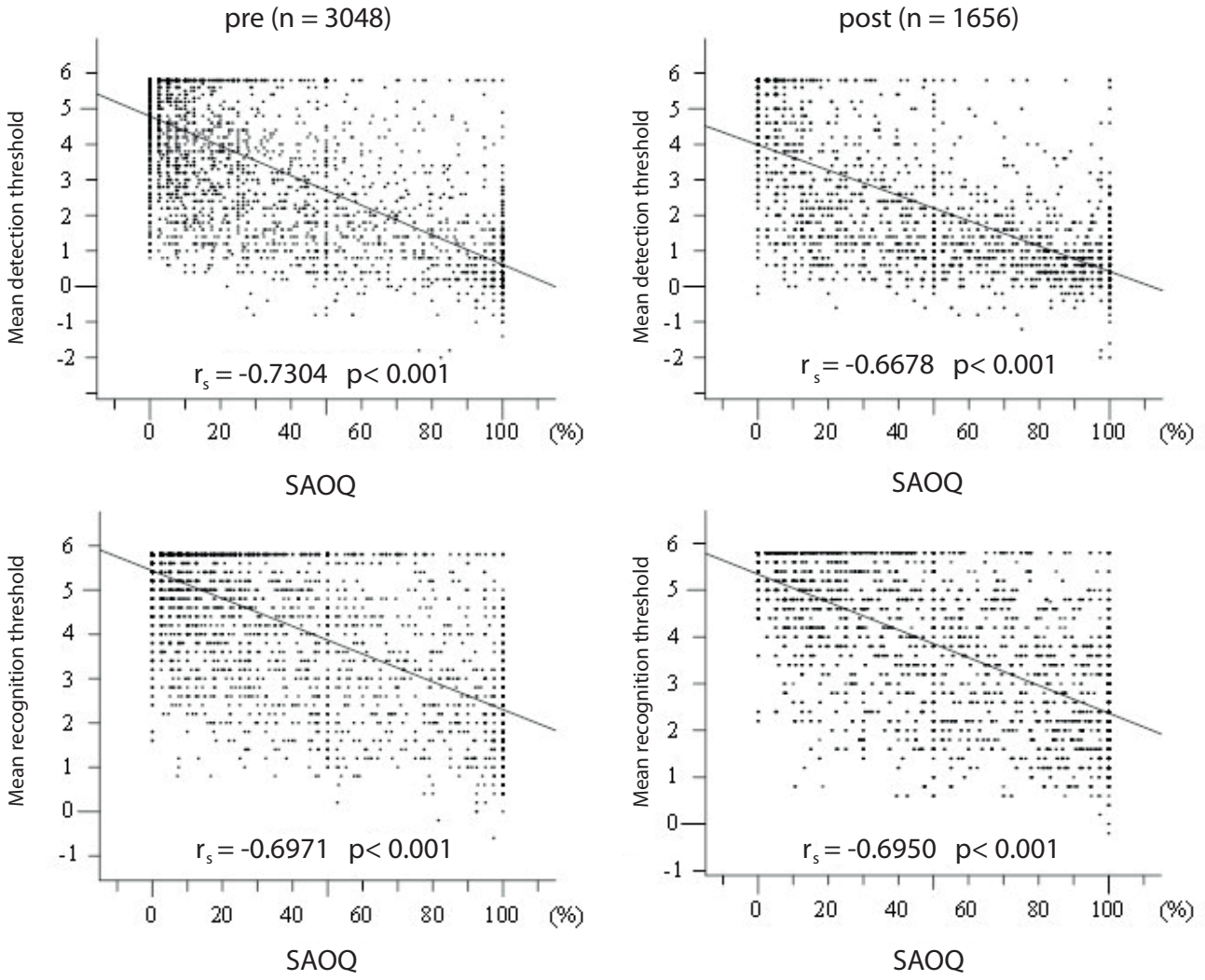


Figure 1. Correlations of SAOQ with olfaction test in total. The SAOQ score significantly correlated with olfactory thresholds (DT and RT) using the olfaction test in both the pre- and post-treatment stages. SAOQ: self-administered odour questionnaire; DT: detection threshold; RT: recognition threshold.

of questions about the following 20 odours: 'steamed rice, miso, seaweed, soy sauce, baked bread, butter, curry, garlic, orange, strawberry, green tea, coffee, chocolate, household gas, garbage, timber, sweat, stool, flower, and perfume' [14]. These 20 odours were carefully selected based on previous studies of olfaction [19]. To answer the SAOQ, patients marked each odour at one of four levels based on their recent memories: two (2) points when they could smell the odour, one (1) point when they could smell the odour occasionally, zero (0) points when they could not smell it at all, and 'not recently smelled or never smelled' (with no counted). 'Not recently smelled or never smelled' odour item was excluded from the scoring, so that 2 points by one 'not recently smelled or never smelled' item were subtracted from denominator. The proportion (%) of the total score for each odour compared with the full score was calculated as the SAOQ score. A higher SAOQ score indicated a better subjective sense of smell. The cutoff value of the SAOQ was statistically calculated as 66.7% with a sensitivity of 99.0% and a specificity of 90.1%, based on a conventional receiver-operating characteristic (ROC) curve and the area under the curve (AUC) analysis, in the previous study [14]. Considering the clarity and practicality of clinical application, we decided on the cutoff value of 70% to facilitate understanding of more accurate values suggesting OD. Patients who answered 'not recently smelled or never smelled' to more than 11 odours were excluded from the analysis.

The SAOQ was first conducted at the first visit in all patients, and then every three months after the start of treatment. In the patients who had evaluable results on both pre- and post-treatment questionnaires, therapeutic reactivity, that is, the difference in the SAOQ score between pre- and post-treatment, was analysed. The most recent data on post-treatment data was used. Changes in SAOQ were not analysed in congenital OD

Table 1. Correlations of SAOQ with olfaction test by causative disease.

	Pre-treatment			Post-treatment		
	n	rs	p-values	n	rs	p-values
Total	3048	-0.7304 -0.6971	< 0.001 < 0.001	1656	-0.6678 -0.6950	< 0.001 < 0.001
CRS	1315 (43%)	-0.7724 -0.7548	< 0.001 < 0.001	673 (41%)	-0.6165 -0.6207	< 0.001 < 0.001
PV	761 (25%)	-0.6719 -0.6399	< 0.001 < 0.001	531 (32%)	-0.6236 -0.6586	< 0.001 < 0.001
PT	183 (6%)	-0.6647 -0.6283	< 0.001 < 0.001	93 (6%)	-0.7899 -0.7601	< 0.001 < 0.001
CNS	53 (2%)	-0.8300 -0.7862	< 0.001 < 0.001	27 (1%)	-0.8686 -0.7712	< 0.001 < 0.001
PNS	52 (2%)	-0.8456 -0.7797	< 0.001 < 0.001	23 (1%)	-0.7351 -0.6091	< 0.001 < 0.001
Congenital	37 (1%)	-0.7549 -0.6593	< 0.001 < 0.001	not tested		
Psychogenic	39 (1%)	-0.7123 -0.5378	< 0.001 < 0.001	not tested		
Idiopathic	608 (20%)	-0.7039 -0.6692	< 0.001 < 0.001	309 (19%)	-0.6946 -0.5938	< 0.001 < 0.001

Re-tests were not performed in patients with congenital or psychogenic ODs. Upper lane, mean detection threshold; lower lane, mean recognition threshold; OD, olfactory dysfunction; SAOQ, self-administered odour questionnaire; CRS, chronic rhinosinusitis; PV, post-viral; PT, post-traumatic; CNS, central nervous system dysfunction; PNS, peripheral nervous system dysfunction.

after definitive diagnosis or in psychogenic OD after treatment because of poor reproducibility.

Furthermore, to investigate the characteristics of each itemised odour, the average score was calculated and compared for each causative disease in the pre-treatment stage. First, the causative disease with the lowest score for each odour item was identified. Significant differences between the lowest disease score and the scores of the other causative diseases were analysed. Smell sensation for each odour item according to disease was determined as 'declined' when no significant difference was detected and as 'preserved' when a significant difference was detected.

T&T olfactometer recognition threshold test

The standard olfactory test using a T&T olfactometer (Takagi and Toyota, which is covered by health insurance in Japan) was used to evaluate olfactory acuity [3]. The T&T olfactometer consists of five odourants: (i) β-phenyl ethyl alcohol, which smells like a rose; (ii) methyl cyclopentenolone, which smells like burning; (iii) isovaleric acid, which smells like sweat; (iv) γ-undecalactone, which smells like fruit; and (v) skatole, which smells like garbage (Daiichi Yakuhin Sangyo Co., Ltd. Tokyo, Japan). The reagents have 8-staged concentration (from -2 to 5) in A, C, D, and E and 7-staged concentration (from -2 to 4) in B. The maximum concentrations of A5, B4, C5, D5, and E5 are 631, 25.1, 100, 795, and 79.5 (mg/ml), respectively. Each reagent was diluted ten times at every stage to the most diluted stage (-2).

Patients were given a paper filter (width, 7 mm; length, 140 mm) dipped into an odour reagent on one side of the tip [15]. Patients sniffed the paper filter at a distance of 10–20 mm through the nostrils. This test kit was used to determine the detection and recognition thresholds (DT and RT, respectively) for each odourant in increasing concentrations. DT was defined as the lowest concentration detectable by the patients, whereas RT was defined as the lowest concentration at which the odour could be identified. Subsequently, DT and RT in the five odourants were averaged, and the mean values were used to evaluate the olfactory acuities. A lower value indicated a higher threshold. The severity of OD was determined based on the values of RT and classified into five groups: (i) normosmia (≤ 1.0); (ii) mild- (1.2 - 2.4); (iii) moderate- (2.6 - 4.0); (iv) severe-hyposmia (4.2 - 5.4); and (v) anosmia (5.6 ≤ RT) [3].

As well as the SAOQ, this test was first conducted at the first visit in all patients, and then every three months after the start of treatment, and the most recent data on post-treatment data was used. Changes in DT and RT were not analysed in congenital OD after definitive diagnosis or in psychogenic OD after treatment because of poor reproducibility.

Statistical analysis

Spearman's rank correlation coefficient was used to analyse

Table 2. Therapeutic changes in SAOQ, DT, and RT.

		Pre-treatment	Post-treatment	p-values
Total	SAOQ	13.2 (0-100)	46.0 (0-100)	< 0.001
	DT	3.8 (-2.0-5.8)	1.6 (-2.0-5.8)	< 0.001
	RT	5.2 (-0.6-5.8)	4.2 (-0.2-5.8)	< 0.001
CRS	SAOQ	37.5 (0-100)	70.0 (0-100)	< 0.001
	DT	3.4 (-2.0-5.8)	1.4 (-2.0-5.8)	< 0.001
	RT	5.0 (-0.6-5.8)	3.8 (-0.2-5.8)	< 0.001
PV	SAOQ	7.5 (0-100)	43.3 (0-100)	< 0.001
	DT	3.5 (-0.6-5.8)	1.2 (-0.8-5.8)	< 0.001
	RT	5.0 (0.6-5.8)	3.8 (0.6-5.8)	< 0.001
PT	SAOQ	0 (0-100)	5.7 (0-100)	< 0.001
	DT	5.8 (-0.2-5.8)	4.0 (-1.6-5.8)	< 0.001
	RT	5.8 (1.8-5.8)	5.8 (0.8-5.8)	< 0.001
CNS	SAOQ	21.4 (0-100)	16.7 (0-100)	0.2710
	DT	3.8 (-1.8-5.8)	3.8 (0.0-5.8)	0.1931
	RT	5.8 (1.4-5.8)	5.8 (1.0-5.8)	0.9193
PNS	SAOQ	19.0 (0-100)	22.5 (0-100)	< 0.01
	DT	2.6 (-1.4-5.8)	2.6 (0.0-5.8)	< 0.001
	RT	5.1 (0.6-5.8)	4.8 (1.2-5.8)	< 0.01
Congenital	SAOQ	0 (0-91.7)		
	DT	5.8 (1.4-5.8)	not tested	
	RT	5.8 (2.4-5.8)		
Psychogenic	SAOQ	27.5 (0-100)		
	DT	2.6 (-0.8-5.8)	not tested	
	RT	4.4 (0.8-5.8)		
Idiopathic	SAOQ	9.4 (0-100)	18.3 (0-100)	< 0.001
	DT	4.1 (-0.6-5.8)	2.6 (-1.0-5.8)	< 0.001
	RT	5.6 (0.8-5.8)	5.0 (0.6-5.8)	< 0.001

Post-treatment SAOQ scores, mean detection, and mean recognition thresholds showed significant improvements compared to those before treatment, except for CNS OD. Data are presented as median (range). SAOQ, self-administered odour questionnaire; DT, detection threshold; RT, recognition threshold; CRS, chronic rhinosinusitis; PV, post-viral; PT, post-traumatic; CNS, central nervous system dysfunction; PNS, peripheral nervous dysfunction; OD, olfactory dysfunction.

the correlation between the SAOQ and the standard olfaction test. Differences in the scores before and after treatment were analysed using the Wilcoxon signed-rank sum test. The Mann-Whitney U test was used to compare the groups of OD severity. Dunn's test was used to compare the odour with the lowest SAOQ score with other odours before treatment. Data are presented as median values (range) unless otherwise indicated. All p-values were two-sided, and values of $p < 0.05$ were considered significant. All statistical analyses were performed using the Stat Flex version 7.0 software (Osaka, Japan).

Results

Relationship between the SAOQ and the olfaction test

Causative diseases of OD were classified as CRS in 1315 (43%) patients, followed by PV in 761 (25%), PT in 183 (6%), CNS in 53 (2%), PNS in 52 (2%), congenital in 37 (1%), psychogenic in 39 (1%), and idiopathic in 608 (20%) patients.

The results of the SAOQ and olfaction tests showed significant

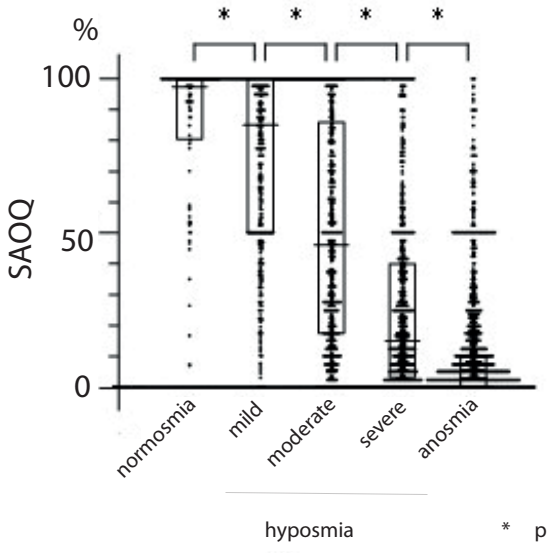


Figure 2. Severity of OD. The SAOQ scores significantly declined as OD severity determined by RT became more severe. Asterisks indicate significant differences ($p < 0.01$). OD, olfactory dysfunction; SAOQ, self-administered odour questionnaire; RT, recognition threshold.

Table 3. Analysis of itemized odours.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
CRS																				
PV																				
PT																				
CNS																				
PNS																				
Con																				
Psy																				
Idio																				

Black boxes indicate the lowest score for each odour item in the causative diseases. Grey and white boxes indicate odour items determined as 'declined' (non-significant difference) and 'preserved' ($p < 0.05$) by statistical comparison with the lowest score (black), respectively. Congenital OD, followed by PT OD, had the highest (black), whereas CRS had the lowest. 'Strawberry' was the most 'declined' (grey) odour item, while 'perfume' was the most 'preserved' (white). CRS, chronic rhinosinusitis; PV, post-viral; PT, post-traumatic; CNS, central nervous system dysfunction; PNS, peripheral nervous system dysfunction; Con, congenital; Psy, psychogenic; Idio, idiopathic; OD, olfactory dysfunction. 1: steamed rice, 2: miso, 3: seaweed, 4: soy sauce, 5: baked bread, 6: butter, 7: curry, 8: garlic, 9: orange, 10: strawberry, 11: green tea, 12: coffee, 13: chocolate, 14: household gas, 15: garbage, 16: timber, 17: sweat, 18: stool, 19: flower, 20: perfume.

correlations before and after treatment (Figure 1). SAOQ scores correlated with olfactory thresholds (DT and RT) in all OD diseases (Table 1). In the analysis for each disease, the results of the SAOQ score, DT, and RT did not show any significant differences between CNS and idiopathic ODs.

The therapeutic reactivity of the SAOQ and olfaction test, post-treatment SAOQ scores, mean DT, and RT showed significant improvements compared to before treatment, except for CNS OD (Table 2).

The severity of olfactory acuity determined using RT was analysed (Figure 2). The median (range) SAOQ scores in the normosmia (n = 95), mild (n = 392), moderate (n = 537), severe hyposmia (n = 656), and anosmia (n = 1368) groups were 97.5% (7-100), 85.0% (0-100), 46.2% (0-100), 15.0% (0-100), and 0% (0-100), respectively. The median SAOQ scores significantly declined in the more severe group.

Deviation groups were defined as normosmic patients with SAOQ cutoff values less than 70% and anosmic patients with SAOQ of 70% or more. Only 2% (31/1368) of the patients with anosmia were divergent, whereas 20% (19/95) of the normosmic patients were divergent. Psychogenic OD was most frequently observed in the deviation groups.

The lowest odour scores in the SAOQ

The causative disease with the lowest score for each odour item was identified (Table 3). Congenital OD had the most odour items, with the lowest score in 14 out of the 20 odours, indicating the worst subjective smell sensation among the causative diseases. PT OD, with the lowest score in 6 out of the 20 odours, was the next most common disease. In CRS OD, all odour scores were significantly higher (better) than those of the other causative diseases. The results of itemised odour in CNS and idiopathic ODs showed similar tendencies.

We analysed whether the smell sensation for each odour item was 'declined' or 'preserved' in the causative diseases by statistical comparison with the lowest scores. 'Strawberry' was the most 'declined' odour item except in CRS OD, while 'perfume' was the most 'preserved' except in PT OD.

Discussion

This study demonstrated that the SAOQ is a clinically useful scoring system for evaluating sense of smell. The results of more than 3000 patients from our clinical practice spanning 17 years confirmed significant correlations the severity of olfactory thresholds between the SAOQ and the gold standard olfaction test in Japan. Analysis of the itemised odour scores showed that 'strawberry' was the most declined-odour, and 'perfume' was the most preserved odour in patients with OD.

The frequency of the causative diseases of OD found in this study, which was highest for CRS followed by PV and PT, is consistent with that previously reported [2,3]. Of note, idiopathic OD accounted for 20% of OD patients. The present survey involved patients with loss of smell at a tertiary medical institution and these findings may not be generalizable. Large national or global surveys may reveal different actual frequencies of OD causative diseases.

In medical environments where olfactory tests cannot be performed, a questionnaire is one of the easiest ways to evaluate loss of smell, even though a questionnaire is not an actual olfactory test and relies on the patient's memory. Because of the limited

use of the olfaction test in Japan, even in the ENT clinic, we proposed the SAOQ as a simple and practical test for the evaluation of olfaction. To quantify the numerical values and analyse the differences, we introduced the concept of a scoring system into the questionnaire assessing smell sensation. The SAOQ had a statistically valid cutoff value of 70% based on data from volunteers without OD and patients with OD in a previous study [14]. This study applied the SAOQ to patients in clinical practice and confirmed its usefulness.

Significant correlations between the SAOQ and olfactory thresholds (DT and RT) before and after treatment suggest that the SAOQ is a useful index for assessing therapeutic efficacy. Correlations of SAOQ with DT and RT imply awareness and actual experience of odours in daily life, respectively. Responsiveness to treatment is a requirement for a well-validated questionnaire. Changes in the SAOQ score after treatment indicate that the SAOQ can be useful for evaluating responsiveness to treatment, as well as olfactory thresholds examined in all causative diseases except congenital and psychogenic OD.

As a next step in this study, we focused on patients with discrepancies between SAOQ scores and olfactory severity, although the SAOQ score reflected the degree of smell sensation. Divergence was observed in 2% of anosmic patients (underestimation) and 20% of normosmic patients (overestimation). The major cause of the deviation groups was thought to be dysosmia, according to interviews before treatment. In our view, the requirement of modifying the SAOQ to evaluate dysosmia is suggested, while the SAOQ might be a more useful screening tool for qualitative OD patients.

In terms of itemised odour analysis, similar results were observed in patients with CNS and idiopathic ODs. It has been suggested that idiopathic OD may include some patients with CNS OD [15]. 'Strawberry' showed the lowest score in the SAOQ, and 'perfume' significantly showed the highest score. The fact that strawberries are seasonal odours and perfumes are odours used daily may have influenced the results. In addition, ester compounds of the main components of strawberry scent, such as furaneol, can control the balance of autonomic nerves and hormones by directly acting on the limbic system and hypothalamus via the olfactory signalling pathway [20,21]. Because of the trace amount, people may perceive the strawberry scent to be weak. Perfume, however, emits a pleasant fragrance and is thought to be strongly related to a better response to the questionnaire. In the elderly, patients with Alzheimer's disease had more severe OD than elderly people without dementia, and low perception of certain aromas, particularly India ink, rose, roasted garlic, Japanese cypress, and wood, was observed in Alzheimer's disease [22]. The Jonckheere-Terpstra test showed significant dementia progression-associated trends of decline in the identifiability of six odourants (perfume, rose, Japanese cypress, curry, India ink, and gas leak odour) [23]. Four odourants (Japanese orange, India ink, menthol, and curry) were identified as significantly associated with the trend for the Study of Osteoporotic Fractures of robust, pre-frail and frail status [5]. These phenomena should be further clarified and explained in terms of the chemical structures of the main fragrance ingredients in each odour in the next research.

This study has some limitations. The SAOQ is a measure of quantitative OD, not qualitative OD, such as dysosmia, including parosmia, troposmia, and phantosmia. Integrating the concept of assessment of OD patients' QOL into a questionnaire is also required [24,25]. A requirement for modifying the scoring system to evaluate qualitative OD and QOL is suggested [25,26]. The SAOQ consists of odours that are particularly familiar to the Japanese. This study was conducted at a single centre in Japan in 2005. Multicentre and cross-cultural studies are needed in the future. Currently, the SAOQ is used for patients with OD attending outpatient clinics specialising in olfactory senses. We propose using the SAOQ for health check-ups and in general practice as well as in the ENT clinic because it can contribute to the early detection of OD and the development of strategies to address the OD disease burden.

Conclusions

The SAOQ is a clinically useful scoring system for evaluating sense of smell. The SAOQ was significantly correlated with the severity of olfactory thresholds determined using the gold standard olfaction test in Japan. The SAOQ can contribute to the early detection of OD and solution of disease burdens caused by OD.

Acknowledgements

The authors gratefully acknowledge the help of their technical assistants Ms. Yumi Kida and Ms. Midori Tanide. We would like to thank Editage (www.editage.com) for English language editing.

Funding

This work was supported by Grants-in-Aid for Scientific Research (JSPS KAKENHI Grant Number 20K09700 and 24K12687) from the Japan Society for the Promotion of Science, a Health Labour Sciences Research Grant (H30-Nantitou(nan)-Ippan-016), and Sanofi Research Grants from the Japanese Society of Otorhinolaryngology-Head and Neck Surgery.

Authorship contribution

TH: study design, analysis of data, interpretation of data, drafting of manuscript, and final approval of manuscript; TS (corresponding author): study design, data analysis, data interpretation, manuscript drafting, and final manuscript approval; KO: data collection, analysis of data, and final approval of manuscript; KF: data collection, analysis of data, and final approval of manuscript; KT: study design, interpretation of data, drafting of manus-

cript, and final approval of manuscript.

Ethics approval and consent to participate

This study used a case series design and was approved by the ethics committee of Hyogo Medical University (approval number 1512). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Conflict of interest

The authors declare that they have no competing interests.

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Takahiro Saito, M.D., Ph.D.
Department of Otorhinolaryngology
Head and Neck Surgery
Hyogo Medical University
1-1 Mukogawa
Nishinomiya
Hyogo 663-8501
Japan

Tel: +81-798-45-6493
Fax +81-798-41-8976
E-mail: t-saito@hyo-med.ac.jp