

# Characteristics associated with objective gustatory dysfunction in patients with subjective chemosensory dysfunction

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## Abstract

**Intro:** Evaluation of gustatory dysfunction is important in patients with subjective chemosensory dysfunction, especially for geriatrics. This study investigated the clinical characteristics associated with objective gustatory dysfunction in patients with chemosensory dysfunction. **Methods:** The Medical records of patients who visited the smell and taste center in a tertiary medical center were reviewed. Patients who underwent all the psychophysical olfactory and chemical gustatory function tests and the subjective questionnaire about chemosensory function were enrolled in this study. The clinical characteristics associated with the objective diagnosis of gustatory dysfunction were statistically analyzed. **Results:** A total of 219 patients were enrolled; 180 were objectively diagnosed as having normal gustatory function, and 39 were objectively diagnosed as having gustatory dysfunction. Subjective recognition of gustatory function was not associated with objective gustatory function. Age, sex, objective olfactory function, and the threshold and discrimination scores for the olfactory function test were significant factors in the multivariate analysis. When the patients were further divided according to age, the threshold test scores rather than other subsets in the olfactory function test were significantly associated with objective gustatory dysfunction in patients 60 and older. **Conclusion:** In older adult male patients with olfactory dysfunction, gustatory function should be considered regardless of subjective gustatory dysfunction.

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**Methods:** The Medical records of patients who visited the smell and taste center in a tertiary medical center were reviewed. Patients who underwent all the psychophysical olfactory and chemical gustatory function tests and the subjective questionnaire about chemosensory function were enrolled in this study. The clinical characteristics associated with the objective diagnosis of gustatory dysfunction were statistically analyzed.

**Results:** A total of 219 patients were enrolled; 180 were objectively diagnosed as having normal gustatory function, and 39 were objectively diagnosed as having gustatory dysfunction. Subjective recognition of gustatory function was not associated with objective gustatory function. Age, sex, objective olfactory function, and the threshold and discrimination scores for the olfactory function test were significant factors in the multivariate analysis. When the patients were further divided according to age, the threshold test scores rather than other subsets in the olfactory function test were significantly associated with objective gustatory dysfunction in patients 60 and older.

**Conclusion:** In older adult male patients with olfactory dysfunction, gustatory function should be considered regardless of subjective gustatory dysfunction.

Keywords: Gustatory dysfunction, age, gustatory function test, relationship, olfactory

## Key points

-Objective gustatory dysfunction did not correlate with subjective gustatory symptoms.

-Age, sex (male), DM, and subjective and objective olfactory dysfunctions were significant factors in objective gustatory dysfunction in patients complaining of chemosensory discomfort.

-Among olfactory function test subsets, the threshold score of the olfactory function test was significantly associated with objective gustatory dysfunction in older patients.

## 1. Introduction

Loss of chemosensory function is associated with various conditions, such as natural aging, underlying chronic medical diseases, and neurocognitive disorders.<sup>1</sup> It has been reported that 10.6% of American adults have reported an olfactory dysfunction within the past year, and 23% have had a lifetime of olfactory dysfunction.<sup>2,3</sup> Compared to olfactory dysfunction, the prevalence of gustatory dysfunction is relatively low. Self-reported gustatory dysfunction in the past year has been reported to occur in only 5.3% of American adults, with a lifetime loss of around 18.7%.<sup>4</sup>

Self-reports tend to underestimate the actual prevalence of chemosensory dysfunction.<sup>3,5</sup> It has been reported that the vast majority of patients complaining of gustatory dysfunction have no deficit in the gustatory function test, and the sensitivity of the questionnaire responses in detecting whole-mouth test-based gustatory dysfunction was less than 0.76.<sup>6,7</sup> Furthermore, data regarding the prevalence of gustatory dysfunction show great dissimilarities between studies, the reported rates of generalized ageusia range from 0.84 to below 4% in patients complaining of gustatory dysfunction and up to almost 20% in the healthy population.<sup>8-11</sup> These heterogeneous reports may be due to the lack of standardized gustatory function tests and the substantial effort and expense of preparing the different concentrations of taste stimuli. These limit the clinical application of the test-based gustatory function test and interfere with the early and proper diagnosis of gustatory dysfunction.

It has been reported that gustatory and olfactory functions are intermingled and affect each other. A patient's olfactory function somehow alters the results of their gustatory function test and perhaps reflects confusion between loss of taste and decreased flavor perception secondary to loss of smell.<sup>7</sup> To increase the efficiency and accuracy of diagnosing gustatory dysfunction, understanding the clinical characteristics, other than the subjective recognition of the symptoms associated with the objectively diagnosed gustatory is necessary.<sup>12</sup>

This study sought to identify the clinical characteristics associated with objective gustatory dysfunction, and suggest the meaningful factors clinicians should recognize in diagnosing and managing patients who are potential candidates for a gustatory function test.

## 2. Materials and Methods

### 2.1 Subjects

This manuscript was prepared using the STROBE checklist, and medical records of patients who visited the smell and taste center of \*\*\*\*\* University Hospital between October 2021 and February 2023 were reviewed. The research protocol was reviewed and found to be in compliance with the Helsinki Declaration and was approved by the Institutional Review Board (IRB) of \*\*\*\*\*University Hospital. The IRB authorized the exemption of getting informed consent from the enrolled subjects.

The inclusion criteria were adult patients who visited our clinic with a complaint of olfactory or gustatory dysfunction and performed all the psychophysical olfactory and chemical gustatory function tests and the subjective questionnaire regarding their symptoms.

The exclusion criteria were patients whose subjective recognition of olfactory or gustatory dysfunction could not be identified, who underwent sinonasal surgery, or who had immunological diseases such as malignancy. Patients previously diagnosed with cognitive dysfunction were also excluded from this study.

## 2.2 Olfactory and gustatory function test

All patients underwent a psychophysical olfactory function test, the YSK olfactory function test (YOF) (RHICO Medical Co., Seoul, South Korea). The YOF test is a validated conventional psychophysical olfactory function test composed of three subsets: threshold, discrimination, and identification. The YOF test was performed following the manufacturer's instructions. The threshold-discrimination-identification (TDI) score range from 1 to 36, and the participants' olfactory function outcomes were labeled as normosmia, hyposmia, or anosmia based on the previously reported criteria.<sup>13</sup>

The gustatory function test, which was developed and validated for use with Korean populations, was applied.<sup>14</sup> Briefly, the testing protocol consisted of 30 taste solutions (six concentrations of each of the five tastants: sweet (sucrose with a concentration ranging from 0.0048 to 0.1563 g/mL), bitter (quinine hydrochloride; 0.00005–0.0016 g/mL), salty (sodium chloride; 0.0006–0.0192 g/mL), sour (citric acid; 0.0002425–0.00781 g/mL), and umami (monosodium glutamate; 0.002–0.064 g/mL). A single drop (approximately 40  $\mu$ L) of the taste solution was applied to the middle part of the anterior one-third of the tongue, and between the drops, the patients were told to rinse their mouths with tap water. The 'taste score,' used to evaluate the overall gustatory function, was the sum of the correctly recognized taste thresholds. Patients with a recognition taste score of less than 12 were regarded as having impaired gustatory function.<sup>14</sup>

The subjective questionnaires regarding chemosensory function were obtained on their first visits.

## 2.3 Statistical analysis

The descriptive statistics for the continuous and categorical variables are represented using the mean (with standard deviation) or count (with frequency %), respectively. Statistical differences in the baseline characteristics between the groups were compared using Wilcoxon's rank sum test and Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to identify significant factors that affected the subjective and objective gustatory dysfunction compared with normal function. The explanatory variables for the analysis were age, sex, diabetes, hypertension, smoking, subjective smell, objective smell, threshold, discrimination, identification, and TDI. The final multivariate logistic regression models were derived using a stepwise selection with Akaike information criteria (AIC). Statistical analyses were performed using R version 4.2.2.

## 3. Results

The demographic and clinical characteristics of the enrolled subjects are summarized in Table 1. Table 1 presents the descriptive statistics from the objective test-based gustatory dysfunction perspective. In total, 180 subjects were identified as having normal gustatory function, and 39 were identified as having gustatory dysfunction. The mean age was  $46.0 \pm 18.8$  years in the normal gustatory function group and  $56.5 \pm 18.1$  years in the gustatory dysfunction group. The difference in age between the two groups was statistically significant ( $p = 0.0016$ ). The composition of sex and the prevalence of diabetes mellitus (DM) were statistically significant ( $p = 0.001$ ). The prevalence of hypertension and the proportion of smokers were not different between the two groups.

Regarding subjective olfactory function, the proportions of subjective normosmia, hyposmia, and anosmia in the normal gustatory function group were 8.3%, 20%, and 71.7%, respectively. In the gustatory dysfunction group, the proportions of subjective normosmia, hyposmia, and anosmia were 38.5%, 25.6%, and 35.9%, respectively. There was a statistically significant difference between the two groups ( $p < 0.0001$ ). Regarding objective test-based olfactory function, the proportions of normosmia, hyposmia, and anosmia were 43.3%, 18.3%, and 38.4%, respectively, in the normal gustatory function group. In the gustatory dysfunction group, the proportions of normosmia, hyposmia, and anosmia were 46.2%, 33.3%, and 20.5%, respectively. There was

a statistically significant difference between the two groups ( $p = 0.041$ ). The mean threshold, discrimination, identification, and TDI scores also significantly differed between the two groups ( $p < 0.0001$ ).

Next, the relationships between objective gustatory function and the other variables were evaluated. Among the exploratory variables, age, sex (male), DM, subjective olfactory function, threshold, discrimination, identification, and TDI scores were significantly associated with the presence of objective gustatory dysfunction in the univariate analysis (Table 2). In the multivariate analysis, age, sex, objective olfactory function, threshold, and discrimination score were selected based on the AIC criteria. Age, sex (male), and objective olfactory function were positively associated with objective gustatory dysfunction, and the threshold and discrimination score were negatively associated with objective gustatory dysfunction. However, when the relationships between subjectively recognized gustatory function and other variables were evaluated, smoking ( $p = 0.028$ ) and subjective olfactory function ( $p = 0.007$ ) were positively associated with subjective gustatory dysfunction in the univariate and multivariate analyses (Supplementary Table 1). Figure 1 shows the violin plots for the continuous variables (age, threshold, discrimination, identification, and TDI) for the objective gustatory function. As shown by the mean and variance information in Table 2 and Supplementary Table 2, there were no significant differences among the continuous variables for subjective gustatory dysfunction (Figure 1A). However, for the test-based objective gustatory function, differences were observed in all the continuous variables (Figure 1B). Significant differences were observed in the threshold, discrimination, identification, and TDI. This was confirmed by the fact that the  $p$ -values for these variables were less than 0.0001 (Table 2).

Finally, the relationships between objective gustatory function and other clinical variables were investigated according to age (age  $\geq 60$  years and age  $< 60$ ). Since there were only two patients with hypertension in the under 60 group, the logistic regression did not converge, and hypertension was excluded from the analysis. In the group aged less than 60, subjective olfactory function, threshold, discrimination, identification, and TDI score were significant variables in the univariate analysis, and sex (male) ( $p = 0.046$ ) was positively associated with objective gustatory dysfunction and the threshold score ( $p = 0.013$ ) and discrimination score ( $p = 0.010$ ) were negatively associated with objective gustatory dysfunction in the multivariate analysis. In the group aged  $\geq 60$  years, sex (male), subjective olfactory function, threshold, identification, and TDI score were significant variables in the univariate analysis. Sex (male) ( $p = 0.012$ ) was positively associated with objective gustatory dysfunction, and the threshold score ( $p = 0.0312$ ) was negatively associated with objective gustatory dysfunction in the multivariate analysis (Table 3).

#### 4. Discussion

This study found that old age, sex (male), DM, subjective olfactory dysfunction, and objective diagnosis of olfactory dysfunction were associated with the objective test-based diagnosis of gustatory dysfunction by the univariate analysis, and old age, sex (male), and objective diagnosis of olfactory dysfunction were significant factors in the multivariate analysis. Additionally, it found that in subjects aged 60 years or older, the threshold score was more significantly correlated with the objective diagnosis of gustatory dysfunction rather than the other subsets in the olfactory function test or a diagnosis of olfactory dysfunction based on the TDI score. It has been reported that subjective recognition of gustatory function did not correspond to the gustatory function test-based objective gustatory function.<sup>6</sup> Similarly, subjective recognition of gustatory dysfunction was not associated with the objective diagnosis of gustatory dysfunction in this study. Furthermore, the characteristics associated with subjective gustatory dysfunction differed from those with objective gustatory dysfunction (Table 2, Supplementary Table 1). Therefore, other referencing characteristics, except for patient discomfort, associated with objective gustatory dysfunction are important for clinicians to determine the application of the gustatory function test.

Variable factors, including endocrinological problems, are known to be associated with gustatory dysfunction.<sup>12, 15</sup> It was found that the prevalence of xerostomia was 46.09% among diabetic patients, and salivary flow rates were lower in DM patients than in non-DM patients.<sup>16</sup> DM disturbs the hemostasis of the oral cavity by altering salivary function and composition even in well-controlled patients and increases the risk of burning mouth syndrome.<sup>17</sup> Although the exact pathogenic mechanisms have not been identified,

these factors could affect the gustatory function in diabetic patients. We suggest that care should be applied to DM patients regarding gustatory dysfunction regardless of subjective complaints of gustatory dysfunction.

It has been reported that with the increase in age, gustatory function tends to decrease, and studies have reported an age-related decrease in taste function.<sup>8</sup> This study also found that age was significantly associated with objective gustatory dysfunction. The interesting finding of this study was that the association between objective olfactory function and objective gustatory dysfunction was different between subjects aged less than 60 years old and subjects aged 60 years and older (Table 3). In the older patients (age  $\geq$  60), the threshold score of the olfactory function test was significantly associated with objective gustatory dysfunction rather than other subsets and the final diagnosis of olfactory dysfunction. However, in patients under 60, the final diagnosis of olfactory function based on the TDI score was significantly associated with objective gustatory dysfunction. Among the olfactory function subsets, performance on the odor identification tests is dependent on verbal abilities, and the results can be influenced by cognitive and language functions.<sup>18</sup> Although this study excluded patients previously diagnosed with cognitive impairments, there is a possibility that in the older subjects, naturally occurring cognitive impairments could have affected the odor identification test, causing low identification, TDI scores, and the final diagnosis of olfactory dysfunction. Therefore, we suggest that in older patients, the threshold subset score should be carefully reviewed when interpreting olfactory function tests, and clinicians should consider performing a gustatory function test regardless of the patient's subjective symptoms.

In this study, the prevalence of objective gustatory dysfunction in patients subjectively complaining of chemosensory dysfunction was 17.8% (39 out of 219 patients). In a previous study, Deems et al. reported that the prevalence of taste loss was 8.7% among patients with complaints concerning smell and taste.<sup>9</sup> These studies imply that a few subjects who complained of chemosensory discomfort were objectively diagnosed with gustatory dysfunction. However, the results of these studies on gustatory dysfunction are heterogeneous, which might be due to the heterogeneity of the applied gustatory function test. This study applied the chemical gustatory function test based on the various concentrations of five taste solutions and the application of the solutions. The study by Deems et al. utilized a whole-mouth test, which used suprathreshold concentrations of liquid taste solutions.<sup>9</sup> Filter paper discs/strips impregnated with a taste solution are also frequently utilized in other countries.<sup>19</sup> Although these chemical gustatory function tests are regarded to be 'objective' function tests, there is a possibility that these are not really 'objective' tests. These tests enable the numerical measurement of gustatory function and are objectively compared with a patient's subjective complaints. However, subjective factors, such as a patient's will, could be involved during the test procedure. Furthermore, there was a previous study where the correlation level was low even among the currently applied 'objective' gustatory function tests.<sup>20</sup> Although more objective gustatory function tests, such as a functional MRI or gustatory evoked potentials, have been introduced, they cannot be commonly applied in the usual clinical field.<sup>9,17</sup> Future studies with larger populations based on a single gustatory function test procedures are needed to suggest further the actual prevalence and characteristics of objective gustatory dysfunction in patients with subjective chemosensory impairments.

This study has several limitations. First, this was a retrospective study based on electronic medical records. Second, this study did not consider all possible candidate factors that could have affected objective gustatory dysfunction. Although the study tried to collect a lot of information, including previously diagnosed medical history and smoking history, other factors, such as burning mouth syndrome and previous medication histories, were not evaluated. Finally, a chemical gustatory function test, which only diagnosed the patient's quantitative function, was applied. Since the currently applied gustatory function test sums up the score of five taste solutions, the final diagnosis was based on the summed recognition threshold score. Therefore, qualitative gustatory dysfunction, such as parageusia, was not considered in this study.

## 5. Conclusion

Objective gustatory dysfunction did not correlate with subjective gustatory symptoms. Age, sex (male), and objective olfactory dysfunctions were significant factors in objective gustatory dysfunction in patients complaining of chemosensory discomfort. Furthermore, the threshold subset score of the olfactory function

test was significantly associated with objective gustatory dysfunction in older patients. We suggest that these characteristics must be understood, and clinicians should apply a gustatory function test in patients who are potential candidates for gustatory dysfunction regardless of subjective discomfort.

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# Tables

**Table 1** . Baseline characteristics and statistical differences between the normal and impaired gustatory function groups

		Normal gustatory function ( <i>n</i> = 180)	Gustatory dysfunction ( <i>n</i> = 39)	<i>p</i> -value
Age	Age	46.0 (18.8)	56.5 (18.1)	0.0016
Sex	Male	108 (60%)	32 (82.1%)	0.01
	Female	72 (40%)	7 (17.9%)	
Diabetes	Yes	9 (5%)	9 (23.1%)	0.001
	No	171 (95%)	30 (76.9%)	
Hypertension	Yes	32 (17.8%)	11 (28.2%)	0.180
	No	148 (82.2%)	28 (71.8%)	
Smoking	Yes	66 (36.7%)	18 (46.2%)	0.281
	No	114 (63.3%)	21 (53.8%)	
Subjective olfactory function	Subjective olfactory function	Subjective olfactory function		<0.0001
Normosmia	Normosmia	15 (8.3%)	15 (38.5%)	0.041
Hyposmia	Hyposmia	36 (20%)	10 (25.6%)	
Anosmia	Anosmia	129 (71.7%)	14 (35.9%)	
Objective olfactory function	Objective olfactory function	Objective olfactory function		
Normosmia	Normosmia	78 (43.3%)	18 (46.2%)	<0.0001
Hyposmia	Hyposmia	33 (18.3%)	13 (33.3%)	
Anosmia	Anosmia	69 (38.4%)	8 (20.5%)	
Olfactory function test	Olfactory function test			
Threshold score	Threshold score	4.18 (2.63)	2.10 (2.28)	<0.0001
Discrimination score	Discrimination score	7.62 (1.82)	5.72 (1.99)	<0.0001
Identification score	Identification score	10.19 (2.61)	7.23 (3.24)	<0.0001
TDI score	TDI score	21.90 (5.28)	15.28 (6.58)	<0.0001

TDI; threshold-discrimination-identification. The counts are given for the categorical variables, and the means (with standard deviations) are given for the continuous variables of the patients.

**Table 2** . Multivariate logistic regression analyses of the demographic and clinical characteristics regarding objectively diagnosed gustatory dysfunction

Parameter	Univariate	Univariate	Multivariate	Multivariate
	Odds Ratio (95% CI)	<i>p</i> -value	Odds Ratio (95% CI)	<i>p</i> -value

Parameter	Univariate	Univariate	Multivariate	Multivariate
Age	1.032 (1.011–1.053)	0.002	1.033 (1.009–1.059)	0.008
Sex	3.048 (1.276–7.278)	0.012	5.849 (2.239–17.335)	0.0006
Diabetes	5.700 (2.093–15.527)	0.0006		
Hypertension	1.817 (0.820–4.025)	0.14		
Smoking	1.285 (0.829–1.992)	0.26		
Subjective olfaction	0.334 (0.213–0.524)	<0.0001		
Objective olfaction	0.763 (0.510–1.142)	0.189	2.047 (1.065–4.302)	0.042
Threshold score	0.650 (0.543–0.778)	<0.0001	0.661 (0.501–0.845)	0.002
Discrimination score	0.605 (0.496–0.738)	<0.0001	0.695 (0.533–0.886)	0.005
Identification score	0.747 (0.669–0.835)	<0.0001		
TDI score	0.851 (0.804–0.901)	<0.0001		

TDI; threshold-discrimination-identification, CI; confidence interval

**Table 3** . Multivariate logistic regression analyses of the demographic and clinical characteristics for objective gustatory function according to age

Parameter	Univariate	Univariate	Multivariate	Multivariate
	Odds Ratio (95% CI)	<i>p</i> -value	Odds Ratio (95% CI)	<i>p</i> -value
Age < 60 years	Age < 60 years	Age < 60 years	Age < 60 years	Age < 60 years
Sex	2.729 (0.754–9.868)	0.13	4.333 (1.149–21.971)	0.046
Hypertension	1.273 (0.269–6.242)	0.77		
Smoking	1.357 (0.723–2.547)	0.34		
Subjective smell	0.274 (0.148–0.509)	<0.0001		
Objective smell	0.695 (0.402–1.200)	0.19	2.463 (0.986–7.726)	0.078
Threshold	0.595 (0.461–0.768)	<0.0001	0.627 (0.417–0.877)	0.013
Discrimination	0.565 (0.434–0.735)	<0.0001	0.629 (0.432–0.880)	0.010
Identification	0.733 (0.632–0.850)	<0.0001		
TDI	0.837 (0.777–0.902)	<0.0001		
Age [?] 60 years	Age [?] 60 years	Age [?] 60 years	Age [?] 60 years	Age [?] 60 years
Sex	5.091 (1.488–17.413)	0.009	5.054 (1.530–20.337)	0.012
Diabetes	2.453 (0.763–7.890)	0.13		
Hypertension	1.130 (0.397–3.212)	0.82		
Smoking	1.206 (0.651–2.232)	0.55		
Subjective smell	0.468 (0.236–0.928)	0.03		
Objective smell	0.907 (0.467–1.761)	0.77		
Threshold	0.728 (0.555–0.955)	0.02	0.736 (0.546–0.959)	0.0312



Parameter	Univariate	Univariate	Multivariate	Multivariate
Discrimination	0.724 (0.525–0.998)	0.05		
Identification	0.796 (0.668–0.948)	0.01		
TDI	0.888 (0.809–0.974)	0.01		

TDI; threshold-discrimination-identification, CI: confidence interval

**Figure legends**

Figure 1. Violin plots for the continuous variables (age, threshold, discrimination, identification, and TDI score) for subjective gustatory function (A) and objective gustatory function (B). To provide more information, small box plots were added inside the violin plots.

