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Correlation between taste and smell alterations and quality of life in patients treated with radiotherapy for nasopharyngeal carcinoma: a cross-sectional study in China

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Abstract

Purpose Taste and smell alterations (TSAs) in nasopharyngeal cancer patients negatively impact their quality of life. This study is aimed at assessing the prevalence of TSAs in patients with nasopharyngeal carcinoma undergoing radiotherapy and at exploring the correlation between TSAs and quality of life.

Methods The research was a cross-sectional survey conducted from June 2023 to March 2024 in which the Taste and Smell Survey (TSS) questionnaires were administered to 135 patients receiving radiotherapy for nasopharyngeal cancer.

Results The mean total score on the TSS scale was 9.37 ± 4.595 . A higher TSS score indicates more alterations. We enrolled 135 patients, 91.1% of whom reported alterations in taste and smell. The severity of alterations was classified as mild (6.7%), moderate (33.3%), and severe (51.1%). The occurrence of changes in taste sensitivity to salty, sweet, sour, and bitter flavors were 66.7%, 52.6%, 52.6%, and 53.3%, respectively, while olfactory sensitivity changes were found in 48.9% of the patients. Notably, a statistically significant correlation was found between cumulative dose of radiotherapy and the TSS score (p < 0.05). TSAs were significantly correlated with anxiety and overall quality of life (p < 0.05).

Conclusion TSAs are prevalent among patients undergoing radiotherapy for nasopharyngeal carcinoma, with the majority experiencing moderate to severe alterations. The findings underscore the importance of implementing targeted interventions to address the sensory alterations and improve the patients' psychological well-being and life quality.

 $\textbf{Keywords} \ \ Nasopharyngeal\ carcinoma \cdot Dysgeusia \cdot Olfactory \cdot Quality\ of\ life$

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Introduction

According to the Global Cancer Report 2022 (Globocan 2022), there were 120,416 new cases of nasopharyngeal cancer and 73,476 associated deaths worldwide [1]. Cases from China accounted for 42.4% of global nasopharyngeal cancer incidence and 38.7% of the related deaths, highlighting a significant disease burden [2]. With rapid advances in modern imaging techniques and the widespread use of linear accelerators, the clinical outcomes for nasopharyngeal cancer have improved substantially, with the 5-year survival rate having risen from 40% in the 1960 s to 70% nowadays [3].

Owing to the deep anatomical location and complex structure of the nasopharynx, radiotherapy, or radiotherapy-based comprehensive treatment, is widely recognized as the most effective radical treatment for nasopharyngeal cancer [4]. However, radiotherapy inevitably irradiates nearby tissues and organs, leading to varying degrees of damage [5]. Taste receptors, located primarily in the taste buds within the papillae on



the dorsum and margins of the tongue, and olfactory receptors, situated in the olfactory epithelium within the olfactory fissure at the top of the nasal cavity, are in close proximity to the tissues irradiated during nasopharyngeal cancer treatment. As a result, taste and smell receptors are highly likely to be exposed to radiation damage. Consequently, taste and smell alterations (TSAs) are highly prevalent among nasopharyngeal cancer patients receiving radiotherapy. These alterations diminish the pleasure and satisfaction patients are expected to derive from feeding, thus leading to appetite loss, reduced food intake, malnutrition, and various psychological challenges ranging from discomfort, anxiety, depression, to diminished social functioning [6–9].

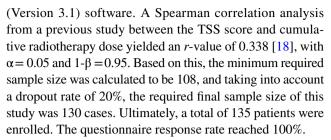
In their study on the relationship among psychology, quality of life, and taste changes in 610 patients undergoing outpatient chemotherapy, Ejder and Sanlier [10] concluded that taste alterations in oncology patients can lead to an inability to taste food, which inevitably causes a significant reduction in food intake. This, in turn, causes weakness, fatigue, and an impaired ability to lead a normal life. Over time, these conditions may trigger feelings of isolation and psychological distress, further diminishing appetite and food consumption. Malnutrition, loneliness, psychological resilience, and altered taste perception are identified as key factors impacting the quality of life in cancer patients. Additionally, a literature review revealed that most studies on the relationship between taste or olfactory alterations and quality of life have focused on patients with head and neck tumors [11], oropharyngeal cancers [12], breast cancers [13–15], lung cancers [16], and advanced cancers [17]. Only limited studies have examined the impact of TSAs on patients with nasopharyngeal carcinoma.

Nasopharyngeal cancer has a higher than global average morbidity and mortality rate in China. This study is aimed at investigating TSAs among Chinese patients undergoing radiotherapy for nasopharyngeal cancer. The objectives were to (1) understand the prevalence and characteristics of these sensory alterations specific to nasopharyngeal cancer, (2) further analyze their correlation with patients' quality of life, and (3) offer a reference for symptom evaluation and potential interventions in nasopharyngeal cancer patients in radiotherapy.

Methods

Participants

A convenience sampling method was employed to select nasopharyngeal cancer patients who met the inclusion criteria and were hospitalized at a tertiary specialized oncology hospital in Sichuan Province, China, from June 2023 to March 2024. The sample size was determined using G*Power



Inclusion criteria: (1) age \geq 18 years, (2) first diagnosis of nasopharyngeal carcinoma confirmed by pathological examination, (3) first radiotherapy treatment initiated, (4) a clear mental state and normal cognitive function, and (5) signed informed consent. Exclusion criteria: (1) insufficient awareness of the disease, (2) preexisting conditions affecting taste or smell prior to treatment, or (3) severe concurrent systemic diseases.

Baseline characteristics

The categories of baseline characteristics were obtained based on a literature review and consultation with clinicians and nurses, including sociodemographic characteristics, treatment-related data, and other relevant characteristics that may affect taste and smell.

Taste and Smell Survey (TSS)

TSS is a widely used scale for the assessment of sensory changes in cancer patients. This scale consists of two sections that address taste changes through nine questions and olfactory changes based on five questions [19]. A patient is considered to experience taste and olfactory changes if they meet any of the following criteria: (1) a response of "yes" to any question regarding taste or olfactory changes; (2) self-reported alterations in the perception of sweet, salty, bitter, or sour flavors, or changes in olfactory sensitivity.

Taste disturbances and olfactory anomalies are scored on a three-point scale, where zero, one, and two indicate minimal impairment, severe impairment, and a total inability to perceive tastes, respectively. Other related issues are scored on a two-point scale, with zero representing no change and one indicating a positive response. The total score ranges from 0 to 16, which categorizes the changes into four levels, namely, 0 to 1: no change, 2 to 4: mild change, 5 to 9: moderate change, and 10 to 16: severe change.

Previous studies have reported an internal consistency reliability of 0.89 [20]. This study involved translating and refining the TSS using expert consultation, with evaluations conducted in two rounds by several medical oncology and nursing experts. Pre-testing was performed among 15 patients with good reliability (internal consistency test coefficient = 0.832).



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Hospital Anxiety and Depression Scale (HAD)

This scale was developed by Zigmond and Snaith [21] in 1983 and has been primarily used to assess anxiety and depression among patients in general hospitals. The HAD is a self-rating scale consisting of 14 items, of which seven items are used to assess depression and the other seven items anxiety. Notably, there are six reverse-scored items (five in the subscale of depression and one in the subscale of anxiety). Each item is scored on a standard scale from zero to three. Annunziata [22] and other researchers have pointed out that, for oncology patients, a score of 9 on the anxiety subscale serves as a cutoff value: scores ≤9 indicate no anxiety, while scores > 9 denote the presence of anxiety, with a sensitivity of 83.1% and specificity of 80.5%. Similarly, for the depression subscale, a score of 7 is used as the cutoff value, where scores ≤ 7 are classified as no depression and scores > 7 suggest the presence of depression, yielding a sensitivity of 72.9% and specificity of 79%.

Quality of Life Questionnaire for Head and Neck Cancer (QLQ-H&N35)

The scale was specifically designed by the European Organization for Research and Treatment of Cancer (EORTC) for patients with head and neck malignancies [23]. Researchers applied the Chinese version of this scale to evaluate the quality of life in patients with nasopharyngeal carcinoma, demonstrating good reliability and validity [24]. The scale consists of 35 items divided into seven domains and 11 individual items. The seven domains include pain, swallowing difficulties, sensory problems, speech issues, eating difficulties, social difficulties, and sexual function. The 11 individual items cover dental problems, difficulty in opening the mouth wide, dry mouth, viscous saliva, coughing, feelings of morbidity, use of pain medications, use of nutritional supplements, use of feeding tubes, weight loss, and weight gain.

Except for five items that employ a binary response format (yes/no), the remaining questions are assessed using a four-point Likert scale, categorized as follows: "No = 0", "Somewhat = 1", "Quite a bit = 2", and "Very much = 3". The scores within each domain are summed and divided by the number of items to obtain a raw score for each domain. This raw score is then converted into a standardized score ranging from 0 to 100, calculated using the formula: Standardized Score (S) = [(Raw Score—0)/Score Range] × 100. The same method can be used to calculate an overall standardized score for quality of life. A higher score for each item or domain or quality of life as a whole indicates more severe symptoms or problems and thus reflects a poorer quality of life.

Data analysis

Data were double-checked, and all the analyses were performed using SPSS version 26.0 statistical software. Categorical data were described using frequency and percentage, while continuous data were presented as mean and standard deviation. Spearman's correlation coefficient, *t*-tests, and analysis of variance (ANOVA) were employed to analyze the relationship between various data and the TSS score. Multivariate analysis was performed using multiple linear regression, and a collinearity analysis was conducted prior to the multivariate analysis to test for correlations among the variables. A *p*-value of less than 0.05 was considered statistically significant.

Results

The influence of baseline characteristics on the TSAs of participants

Results of analyses on basic characteristics of the participants are provided in Table 1, which is split into Table 1(1-1), presenting results of Spearman's correlation analysis of continuous or discrete ordinal data, and Table 1(1-2), presenting results of t-test and ANOVA of categorical data.

According to Spearman's correlation analysis, statistically significant correlations were detected between the TSS score and number of radiotherapy treatments (16.03 \pm 10.061), cumulative dose of radiotherapy (35.03 \pm 22.405 Gy), and number of chemotherapy cycles (3.02 \pm 1.385), respectively (p < 0.05), whereas age (48 \pm 12.071 years), body mass index (BMI), and years of education had no significant influence on TSAs of the patients (Table 1(1–1)). However, significant difference in the TSS score was found among different BMI classifications using ANOVA, as shown in Table 1(1–2) (p < 0.05).

Subsequently, a collinearity analysis was conducted among cumulative dose of radiotherapy, number of radiotherapy treatments, number of chemotherapy cycles, and BMI classification. In collinearity analyses, a variance inflation factor (VIF) above ten of a certain variable indicates high multicollinearity with other variables [25]. The results of our analysis revealed strong multicollinearity of cumulative dose of radiotherapy (VIF = 68.292) and number of radiotherapy treatments (VIF = 68.822) with other variables, while BMI classification (VIF = 1.017) and number of chemotherapy cycles (VIF = 1.236) showed no signs of multicollinearity. Since the number of radiotherapy treatments is inevitably highly correlated with cumulative dose of radiotherapy, a multiple linear regression analysis was performed on cumulative dose of radiotherapy, BMI classification, and number of chemotherapy cycles, with the number of radiotherapy treatments



 Table 1
 Baseline characteristics of the patients

| 1 - 1 The results of Spearman's correlation analy | ysis | | | | |
|---|-----------------|--------------------|--------------------------------------|----------------------|-------------------|
| Variable | | Mean \pm SD | r_S -value | <i>p</i> -value | Total $(n = 135)$ |
| Number of radiotherapy treatments | | 16.03 ± 10.061 | 0.332 | < 0.001 | 135 |
| Cumulative dose of radiotherapy (Gy) | | 35.03 ± 22.405 | 0.349 | < 0.001 | 135 |
| Number of chemotherapy cycles | | 3.02 ± 1.385 | 0.172 | < 0.05 | 135 |
| BMI $(kg/m.^2)$ | | 23.58 ± 3.119 | - 0.125 | 0.149 | 135 |
| Years of education | | 10.29 ± 3.323 | 0.037 | 0.673 | 135 |
| Age (years) | | 48.70 ± 12.071 | 0.037 | 0.670 | 135 |
| 1–2 The results of <i>t</i> -test and ANOVA | | | | | |
| Variable | Total (n = 135) | Percentage (%) | TSS score (Mean \pm SD) | t/F-value | <i>p</i> -value |
| Sex | | | | | |
| Male | 108 | 80.0 | 9.31 ± 4.641 | -0.327^{a} | 0.744 |
| Female | 27 | 20.0 | 9.63 ± 4.482 | | |
| Marital status | | | | | |
| Married | 128 | 94.8 | 9.43 ± 4.609 | 1.110^{b} | 0.354 |
| Unmarried | 5 | 3.7 | 8.40 ± 5.128 | | |
| Widowed | 2 | 1.5 | 8.00 ± 4.243 | | |
| Education level | | | | | |
| Elementary school and below | 26 | 19.3 | 7.15 ± 5.357 | 0.736^{b} | 0.753 |
| Junior high school | 61 | 45.2 | 10.64 ± 3.873 | | |
| Vocational school | 12 | 8.9 | 10.42 ± 4.621 | | |
| College | 21 | 15.6 | 7.71 ± 4.551 | | |
| Bachelor's degree | 13 | 9.6 | 9.92 ± 3.570 | | |
| Graduate degree and above | 2 | 1.5 | 7.00 ± 9.899 | | |
| Occupation | | | | | |
| Employed | 49 | 36.3 | 8.98 ± 4.679 | 0.829 ^b | 0.651 |
| On sick leave | 8 | 5.9 | 7.25 ± 4.097 | | |
| Unemployed | 65 | 48.1 | 9.57 ± 4.831 | | |
| Retired | 13 | 9.6 | 11.15 ± 2.577 | | |
| Tobacco use* | | | _ | | |
| Smoker | 13 | 9.6 | 10.15 ± 4.140 | 0.859 ^b | 0.617 |
| Former smoker | 67 | 49.6 | 9.15 ± 4.425 | | |
| Non-smoker | 55 | 40.7 | 9.45 ± 4.943 | | |
| Alcohol use* | | | ,,,,, | | |
| Drinker | 11 | 8.1 | 10.45 ± 4.824 | 1.645 ^b | 0.068 |
| Former drinker | 69 | 51.1 | 9.87 ± 4.155 | | |
| Non-drinker | 55 | 40.7 | 8.53 ± 5.007 | | |
| Participation in cooking | 33 | 10.7 | 0.55 ± 5.007 | | |
| Yes | 88 | 65.2 | 9.28 ± 4.402 | - 1.168 ^a | 0.303 |
| No | 47 | 34.8 | 9.53 ± 4.982 | 1.100 | 0.505 |
| Sufficient economic resources (self-reported) | ., | 31.0 |).33 <u>+</u> 1.702 | | |
| Yes | 68 | 50.4 | 8.84 ± 4.332 | - 1.360 ^a | 0.456 |
| No | 67 | 49.6 | 8.91 ± 4.820 | - 1.500 | 0.430 |
| Number of chemotherapy cycles | 07 | 49.0 | 0.91 ± 4.020 | | |
| 0 | 4 | 3.0 | 8.75 ± 7.365 | 1.168 ^b | 0.303 |
| 1 | 17 | 12.6 | 6.73 ± 7.363 6.29 ± 5.610 | 1.100 | 0.505 |
| 2 | 24 | 17.8 | | | |
| | | | 10.29 ± 3.884 | | |
| 3 | 39 | 28.9 | 8.62 ± 4.892 | | |
| 4 | 35 | 25.9 | 10.46 ± 3.822 | | |
| 5 | 10 | 7.4 | 11.90 ± 2.514 | | |
| 6 | 6 | 4.4 | 9.17 ± 2.927 | | |



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Table 1 (continued) Disease stage 0.861^{b} 7 0.615 Stage II 5.2 8.14 ± 4.880 Stage III 48 35.6 9.46 ± 4.789 Stage IV 9.43 ± 4.497 80 59.3 BMI classification $< 18.5 \text{ kg/m}^2$ 10 7.4 10.80 ± 3.425 1.738^b 0.049 $18.5 \sim 23.9 \text{ kg/m}^2$ 62 45.9 9.69 ± 4.661 $24 \sim 27.9 \text{ kg/m}^2$ 53 39.3 9.23 ± 4.453 $\geq 28.0 \text{ kg/m}^2$ 10 7.4 6.70 ± 5.458 Radiation therapy plan 0.760^{b} Image-guided radiation therapy (IGRT) 47 34.8 0.727 9.85 ± 4.477 Intensity-modulated radiation therapy (IMRT) 83 61.5 9.08 ± 4.641 Tomotherapy (TOMO) 5 3.7 9.37 ± 4.595

removed. The results showed that only the cumulative dose of radiotherapy had a significant positive effect on the TSS score (p < 0.001), while influence of BMI classification and number of chemotherapy cycles on TSAs was not significant (p > 0.05). Detailed results of the multiple linear regression analysis are shown in Table 2.

Status of taste and smell alterations in the patients

Among the 135 participants, 91.1% reported alterations in taste and smell, among whom the severity of alterations was classified as mild in nine cases (6.7%), moderate in 45 cases (33.3%), and severe in 69 cases (51.1%). Only 12 cases (8.9%) claimed no significant changes. The overall TSS score of the participants was 9.37 ± 4.60 . More information is specified in Table 3.

The correlation analysis between psychological state and TSAs

The results denoted a correlation between the TSAs and the psychological state of patients. More specifically, in the anxiety dimension of the Hospital Anxiety and Depression Scale (HAD), 81 patients (60.0%) reported no anxiety, with an overall score of 7.96 ± 4.79 , while 54 patients (40.0%) claimed to have experienced anxiety, with an overall score of 11.48 ± 3.33 . Spearman's correlation analysis of the anxiety score and the TSS score revealed a statistically significant correlation (r_S = 0.419, p< 0.001). In the depression dimension, 73 patients (54.1%) were classified as non-depressed, with an overall score of 9.07 ± 4.74 ; 62 patients (45.9%) were classified as depressed, with an overall score of 9.73 ± 4.42 . Spearman's correlation analysis of the depression score and the TSS score indicated no statistically significant correlation (r_S = 0.001, p= 0.980).

The correlation analysis between quality of life and TSAs

Table 4 presents the Spearman's correlation analysis between quality of life and the TSAs of the participants. The results indicated a significant correlation between the TSS score and overall score of quality of life. Besides, the TSAs were also found to be correlated with six domains (sensory domain, eating domain, pain domain, dysphagia domain, speech domain, and social domain) and five individual items (the factors of difficulty in opening the mouth wide, viscous saliva, dry

Table 2 The results of multiple linear regression analysis

| Model | Non-standardized coefficients | | Standardized | t-value | <i>p</i> -value | Collinearity statistics | |
|-------------------------------|-------------------------------|----------------|--------------|---------|-----------------|-------------------------|-------|
| | β | Standard error | coefficients | | | Tolerance | VIF |
| (Constant) | 8.564 | 1.581 | , | 5.419 | < 0.001 | | |
| Cumulative radiotherapy dose | 0.070 | 0.018 | 0.342 | 3.869 | < 0.001 | 0.819 | 1.221 |
| BMI classification | -0.878 | 0.497 | - 0.142 | - 1.766 | 0.080 | 0.995 | 1.005 |
| Number of chemotherapy cycles | 0.170 | 0.293 | 0.051 | 0.580 | 0.563 | 0.819 | 1.221 |



^{*}Tobacco/alcohol use: patient with any consumption of tobacco/alcohol within the past 12 months of the survey was defined as "smoker/drinker"; any consumption of tobacco/alcohol 12 months before the survey was defined as "former smoker/drinker"; no consumption of tobacco/alcohol so far was defined as "non-smoker/drinker." at-value. bF-value

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Table 3 Status of TSAs in the patients

| Variable | Total | Percentage (%) |
|---|-------|----------------|
| Foods taste different than they used to | 118 | 87.4 |
| I have noticed a change in my sense of taste | 114 | 84.4 |
| I have had a strange taste in my mouth | 91 | 67.4 |
| The treatment has interfered with my sense of taste | 116 | 85.9 |
| I have noticed a change in salt flavor | 90 | 66.7 |
| Stronger | 36 | 40.0 |
| Weaker | 54 | 60.0 |
| I have noticed a change in sweet flavor | 71 | 52.6 |
| Stronger | 20 | 28.2 |
| Weaker | 51 | 71.8 |
| I have noticed a change in sour flavor | 71 | 52.6 |
| Stronger | 27 | 38.0 |
| Weaker | 44 | 62.0 |
| I have noticed a change in bitter flavor | 72 | 53.3 |
| Stronger | 27 | 37.5 |
| Weaker | 45 | 62.5 |
| Rate abnormal sense of taste | | |
| Insignificant | 29 | 21.5 |
| Mild to moderate | 78 | 57.8 |
| Severe to intolerable | 28 | 20.7 |
| I have noticed a change in my sense of smell | 73 | 54.1 |
| Foods smell different than they used to | 65 | 48.1 |
| The treatment has interfered with my sense of smell | 71 | 62.6 |
| I have noticed a change in odors | 66 | 48.9 |
| Stronger | 32 | 48.5 |
| Weaker | 34 | 51.5 |
| Rate abnormal sense of smell | | |
| Insignificant | 62 | 45.9 |
| Mild to moderate | 45 | 33.3 |
| Severe to intolerable | 28 | 20.7 |

mouth, weight loss, and feeling sick), respectively (p < 0.05). However, scores of other domains and items of quality of life including the sexual domain, dental problems, nutrient solution taken, coughing, use of painkillers, nasal feeding tube, and weight gain were not statistically significant with the TSS score (p > 0.05). More specific results are shown in Table 4.

Discussion

TSAs among patients with nasopharyngeal carcinoma in radiotherapy

The results of this study showed that most cases were experiencing moderate (33.3%) to severe (51.1%) taste and smell alterations. Deshpande et al. [26], in a systematic review and meta-analysis of head and neck tumors, reported that 70–100% of patients experienced partial or total loss of taste sensation during radiotherapy. Similarly,

Li et al. [27] found that 94.2% of patients experienced altered taste sensation. Since TSAs are not life-threatening, healthcare professionals often overlook the assessment and treatment of these symptoms, considering them common post-treatment reactions [28]. Given the high incidence and severity of TSAs in nasopharyngeal cancer patients in radiotherapy, greater attention and intervention from medical personnel are warranted.

As can be seen in Table 3, the taste of salt was the most affected, with a change rate of 66.7%, while the altered taste of sweet, sour, and bitter flavors occurred in approximately half of the participants (52.6%, 52.6%, and 53.3%, respectively). Furthermore, the results demonstrated that reduction was the predominant type of taste alterations. More than half of the participants reported to have experienced a declined ability in the taste of all four flavors, especially in tasting salt.

In contrast, Gunn et al. [29] found that the taste of bitterness was the most significantly affected in patients receiving radiotherapy for head and neck tumors. Asif et al.



Table 4 Correlation analysis of quality of life in different domains/ items and TSS score in patients

| Domains/items of quality of life | Mean ±SD | r_S -value | <i>p</i> -value |
|----------------------------------|-------------------|--------------|-----------------|
| Quality of life | 24.01 ± 10.761 | 0.385 | < 0.001 |
| Sensory domain | 39.14 ± 19.83 | 0.463 | < 0.001 |
| Eating domain | 22.16 ± 16.80 | 0.352 | < 0.001 |
| Pain domain | 25.31 ± 19.83 | 0.309 | < 0.001 |
| Dysphagia domain | 23.39 ± 20.78 | 0.237 | 0.006 |
| Speech domain | 12.18 ± 15.76 | 0.209 | < 0.001 |
| Social domain | 12.79 ± 15.45 | 0.214 | 0.013 |
| Sexual domain | 39.26 ± 26.27 | 0.158 | 0.067 |
| Difficulty in opening mouth wide | 0.39 ± 0.61 | 0.230 | 0.007 |
| Viscous saliva | 1.57 ± 0.94 | 0.205 | 0.017 |
| Dry mouth | 1.57 ± 0.83 | 0.194 | 0.024 |
| Weight loss | 0.47 ± 0.50 | - 0.205 | 0.017 |
| Feeling sick | 1.04 ± 0.76 | 0.203 | 0.018 |
| Dental problems | 0.56 ± 0.71 | 0.129 | 0.136 |
| Intake of nutrient solution | 0.36 ± 0.48 | -0.146 | 0.092 |
| Coughing | 0.50 ± 0.69 | 0.092 | 0.290 |
| Use of painkillers | 0.73 ± 0.45 | 0.007 | 0.937 |
| Nasal feeding tube | 0.89 ± 0.37 | -0.005 | 0.958 |
| Weight gain | 0.90 ± 0.30 | 0.013 | 0.885 |

[30] reported that the taste of sweetness and salt reduced considerably, the bitter taste of bitterness showed a tendency of diminishing, while the taste of sourness remained unchanged. The variability in these results may be attributed to the difference in the cancer type, which lead to varied radiation doses received by the tongue during treatments.

Additionally, 62.6% of nasopharyngeal cancer patients reported that radiotherapy interfered with their sense of smell, a rate similar to the 60% incidence of olfactory changes in head and neck cancer patients reported by a previous study [31]. This rate is higher than the 16-49% incidence of olfactory alterations observed in cancer patients receiving chemotherapy [14]. Olfactory perception plays a critical role in the overall taste experience, but olfactory dysfunction has received less attention than taste alteration and is often misreported as a taste dysfunction. Thus, gradual loss of smell may go unnoticed [32]. The preauricular field is the most commonly targeted area, including the posterior one-third to two-thirds of the nasal cavity, the middle and posterior groups of the ethmoid sinuses, the entire sphenoid sinus, and the preauricular region. This extensive exposure often results in a reduction in olfactory bulb volume and impaired olfactory function [33, 34].

In some cases, olfactory sensitivity either increased (48.5%) or decreased (51.5%) following chemotherapy, and this phenomenon was potentially influenced by sex [20].

Women tend to be more sensitive to taste and smell changes than men. However, nasopharyngeal cancer predominantly affects men, with an incidence rate roughly twice as high as that of women [35]. Given the relatively small sample size of this study, further research with a larger sample size is needed to investigate sex-related differences in TSAs among nasopharyngeal cancer patients.

The impact of radiotherapy on TSAs among patients with nasopharyngeal carcinoma

Results of the multivariate analysis indicated that the cumulative dose of radiotherapy is the main influencing factor of TSAs (p < 0.05, Table 2). Sapir et al. [36] found that the degree of subjective taste loss was significantly associated with the radiation dose to the oral cavity (p = 0.005) and the tongue (p = 0.019). Another study also pointed out that the degree of post-radiotherapy taste loss is positively correlated with radiotherapy dose [37]. Radiotherapy for nasopharyngeal cancer typically targets various regions, including the preauricular, prenasal, infraorbital, face, neck, retroauricular, cranial base, cervical tangential, and upper lateral cervical vertical fields. However, normal surrounding tissues, such as the oral cavity, tongue, and olfactory regions, are also exposed to radiation. Consequently, the degree of taste and olfactory alterations in nasopharyngeal carcinoma patients exacerbates with an increasing number of radiotherapy treatments and cumulative radiation dose. Therefore, it is highly suggested that nursing staff should provide early personal assessments, care plans, and guidance based on the patient's stage of disease and radiotherapy dosage, allowing for an early prediction and intervention of TSAs.

Furthermore, the primary cause of TSAs in nasopharyngeal carcinoma patients in radiotherapy is cellular damage. This damage may result from structural changes of cells, modifications on receptor surfaces, disruption of neural coding, or a reduction in the number of healthy cells [38]. Hence, the degree of taste and olfactory sensitivity alterations varies significantly among individuals. Regarding smell dysfunction as well as specific taste changes in salt, sweetness, sourness, and bitterness, different dietary interventions have been suggested. For patients with hyposmia, adding more seasonings (e.g., salt, sugar, spices, and other condiments) or choosing flavorful foods like mushrooms and onions proves to be helpful [39]. For patients with olfactory dysfunction, incorporating ingredients with a spicy smell and taste such as onion, ginger, garlic, star anise, and cinnamon may help [40]. Nevertheless, in the case of severe TSAs, it is highly recommended for the patient to consult a dietitian for further assessment and dietary modifications so as to prevent nutritional deficiencies. It is also worth noting that current dietary interventions are primarily based on



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chemotherapy-induced TSAs. Further research is urgently needed to determine whether specific dietary interventions vary for different causes of TSAs and to promote the development of more targeted dietary strategies for patients suffering from radiation-induced TSAs.

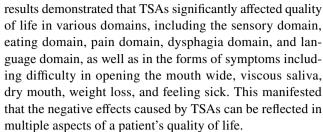
The relationship between TSAs and psychological status in nasopharyngeal carcinoma patients in radiotherapy

Previous studies have indicated that nasopharyngeal carcinoma patients are prone to anxiety and depression during radiotherapy, and the incidence and severity of these conditions are closely associated with age, gender, smoking history, education level, treatment-related toxicity, etc. [41]. Among the treatment-related toxicities, altered taste is frequently linked to anxiety and depression. These discomforts may lead to dissatisfaction and anxiety, which may further exacerbate into heightened anxiety and depression, contributing to a decline in patients' physical functioning and quality of life [42].

Our results showed that 40.0% of the patients experienced anxiety, and 45.9% suffered from depression, which is comparable to the results of a study conducted by Wang et al. [43], who reported the incidence of anxiety and depression as 55.1% and 43.9%, respectively, in nasopharyngeal carcinoma patients undergoing radiotherapy. Our results revealed a significant correlation of TSAs with anxiety ($r_s = 0.419$, p < 0.001) but no correlation with depression. This contrasts with previous findings that both anxiety and depression were associated with acute radiotoxicity in nasopharyngeal carcinoma patients in radiotherapy, with depression being a predictor of taste disturbances and anxiety of vomiting and dysphagia [44]. This discrepancy of the results may be explained by the fact that the focus of our study was on the combined impact of TSAs on psychological status, whereas most existing research has concentrated on the psychological effects of taste alterations alone. Additionally, researchers have also found that more severe taste abnormalities, particularly those associated with oral mucosal clusters, are correlated with lower levels of psychological and environmental comfort [45]. Therefore, healthcare providers should guide patients in adopting effective emotion regulation strategies to mitigate treatment side effects, in order to improve patients' psychological state and, more importantly, their quality of life [46].

The relationship between TSAs and quality of life in nasopharyngeal carcinoma patients in radiotherapy

A significant positive correlation was found between TSAs and quality of life, a finding consistent with the studies by Ying et al. [46] and Wu et al. [47]. More specifically, our



Symptoms such as dry mouth, viscous saliva, difficulty in opening the mouth wide, oral pain, and dysphagia are common among nasopharyngeal cancer patients and are known to affect nutritional status [48]. The results of our study demonstrated that these nutrition-impacting symptoms are correlated with TSAs. Similar conclusions were drawn by Crowder et al. [48] who highlighted the importance of addressing taste disorders to ensure adequate protein and calorie intake, which plays a crucial role in improving the quality of life for head and neck cancer patients. Besides, Thorne et al. [49] emphasized that the assessment of TSAs is essential, as these changes can be associated with other common issues such as weight loss. TSAs are not only significant symptoms but also independent predictors of quality of life, necessitating targeted management by healthcare professionals [11]. Hence, it is critical not only to assess the psychological impact of radiotherapy-induced TSAs but also to evaluate how these changes affect items of quality of life such as pain, and issues concerning feeding, saliva, and mouth, and provide patients with targeted advice. A holistic assessment can to a great extent enhance the care, support, and empathy provided by healthcare staff for the patients. For instance, patients with dry mouth should be advised to drink 2000-3000 ml of fluids per day (light fruit juice and tea included) and to carry beverages at all times to reduce oral dryness, which can effectively mitigate the impact of TSAs on their quality of life [39].

When severe TSAs occur, referral to a dietitian for further assessment and potential dietary adjustments is highly recommended. Additionally, multidisciplinary professionals should proactively inform patients of the possibility of TSAs to alleviate anxiety and depression. Furthermore, providing patients with educational materials on taste change management, dietary counseling, and strategies to enhance food flavor can also help improve eating behaviors and prevent weight loss, ultimately preventing a reduction in their quality of life [49].

Limitations

This is a cross-sectional study with a relatively small sample size, and longitudinal changes in TSAs were not explored. Larger-scale and longitudinal studies in the future will help to further investigate the influence of TSAs on cancer patients specific to tumor type.



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Conclusions

The incidence of taste and smell alterations (TSAs) among patients undergoing radiotherapy for nasopharyngeal cancer is both high and severe, with notable individual variability. Patients frequently experience diminished perceptions of salty, sweet, sour, and bitter tastes and olfactory dysfunction. Additionally, these alterations are associated with heightened anxiety, leading to reduced psychological comfort. Furthermore, TSAs are closely linked to the quality of life in various domains, including pain, dysphagia, and issues concerning speech, sensation, and feeding. Specific symptoms such as difficulty in opening the mouth wide, viscous saliva, dry mouth, weight loss, and feeling sick are also significantly correlated with TSAs.

It is essential for clinical practitioners to assess these alterations comprehensively, not only focusing on the TSAs but also evaluating the broader effects of the alterations on the patient's quality of life in various aspects. Through this, healthcare providers are able to deliver more personalized nursing care, offer more targeted nursing interventions, counseling, and health education aimed at mitigating the adverse effects of TSAs, and ultimately improve the patient's overall quality of life.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This research has been reviewed and approved by the Ethics Committee of the institution, with the ethical approval number SCCHEC- 02–2022 - 078.

Informed consent Informed consent was obtained from the patients.

Competing interest The authors declare no competing interests.

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