

Research Article

Patient Reported Outcomes, Oral Health, Taste and Dietary Impact During and Following Head and Neck Cancer Therapy

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Keywords

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Abstract

Objective: The purpose of this paper is to present patient reported outcomes (PRO) of oral function and toxicity in head and neck cancer (HNC) patients and the clinical oral conditions affecting diet and maintenance of body weight during and following cancer therapy.

Study design: Patients with HNC were evaluated during and following cancer therapy. Oral conditions affecting taste and oral diet, including taste and smell function were assessed.

Results: The participating patients reported appetite decline and taste loss in 50% of patients during and in 62.5% following treatment. Decreased food intake and altered food choice were reported as severe by 50% of patients. Throat and mouth pain affected 67% of acute and 42% of post-treatment patients. The spicy perception of capsaicin was reported to have severe impact for 80% of acute and 70% of post-treatment patients. Bitter taste perception affected oral diet either often or all the time in 33% of acute and in 83% of post-treatment patients. Weight loss occurred in 5% during treatment and in 12% post-treatment.

Conclusions: This is the first report of clinical oral function including taste and smell testing, saliva production and patient reported outcomes. Oral complications including mucositis and saliva affect taste change throughout cancer treatment and in the first two years of survivorship. This study provides initial suggestions that may guide diet and food intake and in product development for HNC patients.

ABBREVIATIONS

CT: Chemotherapy; HNC: Head and Neck Cancer; MDASI-HN: MD Anderson Inventory-Head and Neck; PRO: Patient Reported Outcomes; RT: Radiation Therapy; STTA: Scale of Subjective Total Taste Acuity; VHNSS: Vanderbilt Head and Neck Symptom Survey; WIRB: Western Institutional Review Board

BACKGROUND

Oral intake is impaired during treatment for head and neck cancer (HNC), as oral and oropharyngeal function in patients is negatively affected. Oropharyngeal pain, decreased saliva production, taste and smell changes, and general symptoms of fatigue and nausea influence appetite [1,2]. Flavor is a multidimensional symptom that requires saliva production and is impacted by taste, touch, temperature, and smell. Taken together, these factors affect appetite. Taste qualities include salt,

sweet, sour (acid), bitter, savory (*umami*), fat taste and possibly water taste [3,4]. Spicy foods and foods that cause a cooling sensation also affect the flavor of food [5], by activating receptors of trigeminal neurons. Eating, while a nutrition related activity, also affects social and cultural interactions [3,4].

Dysgeusia may be caused by local injury to mucosa that includes damage to taste or olfactory function, saliva change (quantity and quality), oral infection, and systemic conditions [4,6-9]. Dysgeusia is common in HNC patients [1,4,10,11]. Radiation therapy (RT) has local/regional effects on taste function and chemotherapy (CT) may effect taste and smell [12]. CT may have effects upon taste and smell and has general effects such as fatigue and nausea [4,13].

Changes in taste impacts the quality of life, contributing to morbidity and potentially mortality [9,12,15]. Taste changes and nutritional compromise have been associated with impaired

immune function [15,16]. Patient reported outcomes (PRO), using the MD Anderson Inventory-Head and Neck (MDASI-HN), survey in HNC survivors post-RT with or without CT showed that less than one-third of these patients reported maintaining a normal diet. This study reported that dysphagia and dental problems were associated with diet modifications. Further studies have documented that the experience of eating is altered following HNC therapy, and negative social impact [9,19].

In this prospective study, we examined HNC patients during and following cancer therapy, and assessed PRO, oral examination findings and taste and smell. This report focuses on PRO and correlation with oral examination findings, along with taste/smell testing previously reported [20].

METHODS

Ten patients were evaluated 4-6 weeks after starting HNC therapy (acute treatment group, N = 6), and following treatment (post-treatment group, N = 8). Patients enrolled were adults with HNC, scheduled to receive intensity-modulated RT with/without platinum-based CT and/or HNC patients up to 2 years following cancer treatment. Exclusion criteria included prior treatment for HNC, induction CT and tumor involving more than 50% of the oral tongue.

To assess patient report of treatment toxicities, the Vanderbilt Head and Neck Symptom Survey (VHNS), and the Scale of Subjective Total Taste Acuity (STTA), were completed by the patients. The VHNS v 2.0 evaluates oropharyngeal treatment related toxicities. This data is presented in the results section as a score of 1-2 for the item indicates that the toxicity was present while a score ≥ 4 indicates the toxicity was present and severe [21]. The STTA assesses the overall perception of changes in taste with zero representing no change and four representing almost complete loss of taste function [4]. Taste testing used rapidly dissolving pullulan-based edible films that included a taste or trigeminal stimulus in the film as previously reported [20,22]. Taste intensity was measured on a 7-point Likert category scale (none – strong). Olfactory function was measured with the Smell Identification Test (Sensonics, Haddonfield, NJ).

Descriptive analysis was performed for all variables and are presented as counts with percentages for dichotomous and categorical variables. Age is presented as mean \pm standard deviation. Western Institutional Review Board (WIRB, Puyallup, WA; IRB # 20172768), approved the study and all patients provided written informed consent to participate.

RESULTS

Patient's demographics and clinical characteristics are summarized in Table 1. Tobacco use, defined as >15 pack/year history, was reported by three patients and half of the patients reported social alcohol use, defined as 2-4 drinks/week. Average weight loss of 5% during treatment and 12% at follow-up was seen.

Most patients reported that appetite declined during treatment and at follow-up (Figure 1A). All patients reported very good appetite at the start of treatment, during treatment, 16.7% reported poor or very poor appetite, and following treatment 50% reported poor or very poor appetite.

Food and beverage textures consumed (e.g.: thin liquid, thick liquid, semisolid, soft, firm, hard, abrasive) were reported in the acute and post groups, respectively: all food textures 66.7% and 62.5%; all textures to thick liquids 30% and 60%; and consuming all kinds of liquid/beverage 100% and 60%. Completion of a meal was impacted during treatment and in follow-up. More than half of patients reported eating a whole meal or more to feel full in both groups: 66.7% in the acute group and 62.5% in the post treatment group (Figure 1B). Most patients needed longer or a much longer time to consume a meal: 50% in the acute group and 62.5% in the post group. Pleasure and enjoyment associated with eating prior to cancer treatment, was rated as very pleasant or pleasant by all the patients, while 66% reported unpleasant or very unpleasant eating due to no taste, pain or difficulty swallowing in the acute group and 28.6% in the post treatment group.

Oral symptoms that may affect food consumption during and following HNC treatment are shown. During treatment, throat and mouth/tongue pain due to mucositis was reported by 67% of patients. Following treatment, throat and mouth pain was reported to impact eating in 54% of the early post-treatment visits and by 42% of the post-treatment group. Taste loss was reported by 50% of patients during treatment, and 62.5% of patients following treatment.

Oral symptoms impacting function are shown in Table 2. Dry mouth was rated as severe by 80%, and mild by 20% of patients during treatment and severe by 86% and mild by 14% of post-treatment patients. Thick mucus in the oral cavity had severe effect for 60% and 28% of patients during treatment and post-treatment, respectively. Food sticking in the mouth was reported at follow up to be severe by 72% of patients. In contrast, food sticking in the oral cavity was reported as severe for 40% of patients during treatment.

Taste change during treatment was reported as severe by 67% of patients and mild by 33% and similar report of decreased amount of food consumption was noted in patients during therapy. Altered food choice was reported as severe by 50% of patients and minor by 33%. Following treatment, taste change was reported by 88% of patients with 50% reporting severe effects resulting in decreased food intake and altered food choice 50% of patients.

Table 1: Demographics of study participants.

Patient Number		10	%
Gender	Male	7	70
	Female	3	30
Mean Age (y)		59.9 \pm 7.0	N/A
Ethnicity	Caucasian	8	80
	Hispanic	1	10
	Asian	1	10
Cancer Location	SCC* Tonsil p16 positive	6	60
	Base of Tongue p16 positive	3	30
	Oral Tongue p16 positive	1	10

*SCC refers to oral squamous cell carcinoma.

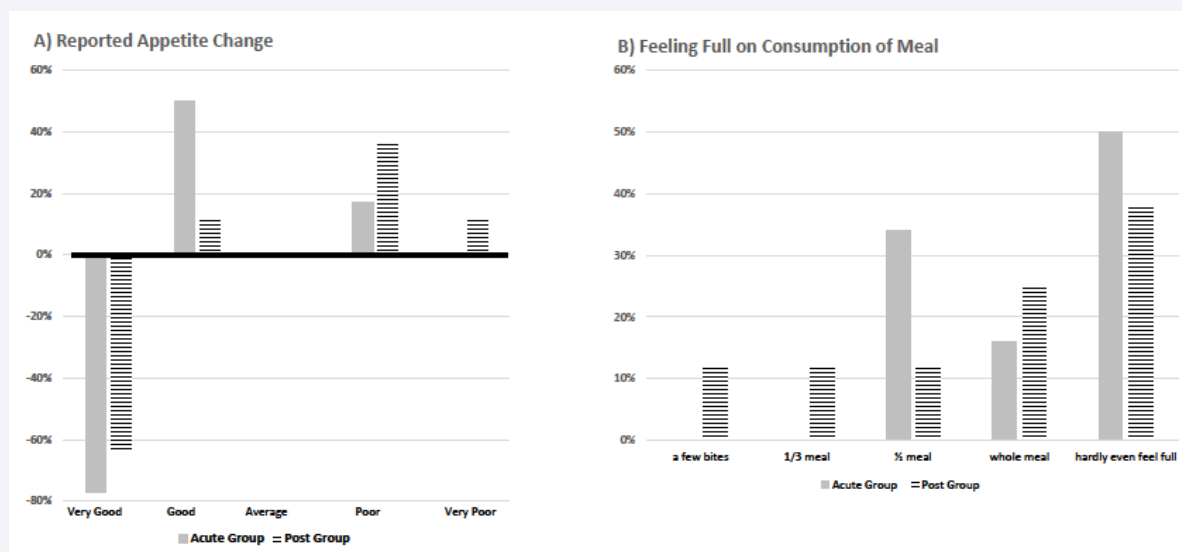


Figure 1 Reported Appetite Change and Feeling Full on Consumption of Meal for Acute and Post Groups.

Table 2: Percentage of Patients Reporting Oral Symptoms that Impacted Diet.

	Acute Group (n = 5)		Post Group (n = 7)	
	≥ 1	≥ 4	≥ 1	≥ 4
Xerostomia				
Xerostomia	20	80	14	86
Excess mucus				
Thick mucus/phlegm	40	60	28	28
Swallowing difficult	40	40	28	56
Mucosal sensitivity				
Sensitive to spicy, hot, or acidic foods	20	80	28	72
Range of motion				
Limitations in jaw movement	20	40	72	14
Swallowing/eating foods				
Food gets stuck in mouth	20	40	14	72
Food gets stuck in throat	60	0	42	42
Choke/strangle on liquids	0	0	58	0
Dental health				
Difficulty chewing due to teeth/dentures	20	0	14	0

Table 2 note: Symptoms can range from 0 (no symptom present) to 10 (most severe report of the symptom), and are categorized as 1-3 for 'symptom is present' and ≥ 4 for 'severe symptom is present'. Within group totals may be less than 100% if a patient(s) reported '0'(no symptom present) for the indicated symptom.

Taste changes also had an impact on food choices (Table 3). In this cohort, spicy sensation and sour taste were the most problematic during and after treatment. The spicy perception of capsaicin was reported to have severe impact by 80% of patients during treatment and 70% following treatment. Bitter taste affected oral diet often or all the time in 33% of patients during treatment, and in 83% following treatment. The following tastes impacts were experienced by 50-60% during treatment but reduced to between 0-28% in post treatment: bland, *umami* (savory), sweet, metallic and fat taste. Smell identification was similar during treatment ($x = 28.33 \pm 6.71$) and post-treatment ($x = 31.00 \pm 7.69$).

DISCUSSION

Acute oropharyngeal complications of HNC therapy include mucositis, pain, saliva change, secondary oral infection, taste change, dysphagia, odynophagia, aspiration, fatigue, nausea, limited jaw opening and tongue movement. Acute complications result in social and psychological effects and are associated with fatigue, depression and isolation [18]. As acute oral complications resolve following treatment, chronic toxicities continue to impact oral and oropharyngeal function. The impact of RT upon taste is multifactorial and is compounded when combined with CT [1,4,17,19].

Table 3: Percentage of Patients Reporting Taste Changes Affecting Food Choices.

Taste	Frequency of impact upon Diet				
	None	Seldom	Half time	Often	All the time
Umami Pleasant					
Acute		40		20	40
Post	28	42		14	14
Bitter					
Acute	40	20			40
Post		17		51	34
Bland					
Acute		40		40	20
Post	42	42		14	
Sour					
Acute	20		20	20	40
Post	42		14	14	28
Sweet					
Acute	20	20		20	40
Post	42		42		14
Salt					
Acute	60	20		20	20
Post	42	28	14		14
Metallic					
Acute	40			20	40
Post	100				
Fatty					
Acute		20		20	60
Post	57	14		14	14

Table 3 note: Acute group n = 5, post group n = 7 except for "bitter" n = 6

A recent survey of HNC survivors reported the most impactful symptoms following treatment include dry mouth, difficulty swallowing, mucus secretion, taste change and choking/coughing while eating [17]. Dysphagia and problems with teeth/gums were associated with maintaining a normal diet [17].

The current study showed that symptoms that affect food consumption differed during and following cancer treatment. During treatment acute toxicities causing mouth and throat pain due to mucositis affected two-thirds of patients and although following cancer treatment, pain was less impactful. Dry mouth was reported in 50% of patients following treatment and was correlated with whole resting saliva ($r = -0.96$, $p < 0.01$) as well as unstimulated saliva in the post treatment group ($r = -0.98$, $p < 0.01$; see [20]). Half of patients reported their eating ability was affected due to food texture in the post-treatment group. Although these changes were not statistically significant, differences throughout the treatment trajectory and following treatment may assist in predicting patient food preferences. These findings suggest that evaluation and management of the oral conditions and modifications of diet and food product development are required to address the trajectory of oral function during and following therapy.

Hyposalivation may limit saliva food-coating and decreased food particle delivery to taste receptors [23]. Hyposalivation and viscous secretions impact oral comfort, taste function, speech and swallowing. Oropharyngeal infection (e.g., candidiasis), affects taste and oral comfort. As previously reported, more viscous (mucus), secretion impact taste function that was found in the

current study [9]. Therefore, saliva quantity and quality should be assessed in HNC patients and managed when possible. Other studies state that saliva change caused by cancer therapy may lead to decreased taste function [9,17,23,24].

Taste change during radiation therapy, typically occurs concurrently with mucosal damage, which suggesting direct damage to taste receptors, while persisting change in taste following treatment may reflect decreased turnover rates of taste receptor cells, and/or neuronal damage [2,17,24,25]. Taste recovery is unpredictable with some patients reporting improvement in a few months to a year after cancer therapy, while others may not fully recover [9,26-28].

In the current study, taste change was reported by all patients during treatment and by 87.5% of participants post-treatment with follow-up continuing up to two years. The changes in taste were associated with decreased amount of food eaten and altered food choices. In addition, taste change impacts diet choice, social aspects of food consumption, and sociocultural influence in people with traditionally spicy diets. These changes appear to represent painful mucositis during treatment and may reflect mucosal toxicity and neuropathy (C-fiber activation), post-treatment. In the post-treatment group, 50% of patients reported their eating ability was affected by food texture but was less common (16.7%), in the acute group. Although these changes were not statistically significant between the two groups, these differences may promote understanding in order to anticipate patient food and meal preferences.

Most patients were challenged in completing a meal and required a longer time to consume a meal. These findings require patient accommodations due to impact upon diet and nutrition and social interaction around meals and support recommendations for smaller portions, snacking and more frequent meals.

As reported in our prior companion paper [20], taste intensity and pleasantness (hedonics), testing with edible taste strips followed a similar pattern as the tastes that impacted food choices, as reported separately for this cohort. Spicy/pungent responses with capsaicin as the stimulus showed the highest (strongest), intensity and most strongly disliked stimulus during treatment and follow up. Fat taste (linoleic acid), and sweet taste (sucralose), were most frequently reported as producing strong intensity during treatment. At follow-up, the most frequently reported intensity for fat taste was moderate, and sweet was variable from weak to strong intensity. Sweet was the only primary taste quality to receive a positive pleasantness (hedonic), rating as the most frequent response. Salt taste stimuli yielded strong intensities during and following HNC treatment, and was most frequently reported as extremely disliked in the follow-up group. These findings inform diet recommendations and product development for people during and following HNC therapy.

Olfactory function may be affected in HNC therapy when RT includes the nasopharynx and the olfactory bulb along with CT [1,16]. Changes in olfactory function have been reported with CT that included cisplatin and methotrexate [16]. However, in our report, only three HNC patients (33%), reported smell disturbance. Of the patients that reported change in smell identification, two were seen approximately 3 to 4 months after treatment with combined RT/CT.

In the current study, all HNC patients in a prior report had moderate to severe taste disturbance and dry mouth as previously reported [9]. Other studies report that 75% to 100% of HNC patients who received RT experience taste change depending on the radiation dose and treatment fields [4,28].

In a prior study, variable changes of reduced or abnormal taste perception occurred in two-thirds of patients, and increased intensity occurred in one third of patients [9]. In addition, taste studies with electrogustometry show taste qualities are affected. HNC patients had a high number of reported "no taste" or "abnormal taste" and a correlation between decreased sweet and increased sour taste [9,29], comparable to findings in the current study. In a recent study, Epstein et al. [9], found that bitter taste function was altered in most HNC, which was reported in the current study particularly post-treatment. As reported in the current cohort [20], sensitivity to spicy and acidic (sour) foods was highly impactful during and following treatment. In prior studies, *umami* taste was the most affected sensation [9,29], which may have an effect upon appetite and oral intake, and decrease in quality of life [30]. In the current study, *umami* taste was reported impactful by 60% of patients during treatment, with fewer reporting impact post-treatment (28%), suggesting some recovery may occur in *umami* taste post-treatment. Fat taste change was reported by 83% during treatment and in 28% following treatment. The potential recovery in *umami* and fat taste over time, reported in this study, may affect dietary

guidance and product development considerations in order to consume high energy foods and maintain enjoyment of eating. Some studies have shown improvement by 8 weeks following HNC treatment [29,31]. However, other studies found that taste changes may persist indefinitely in some HNC patients [1,30]. In the current study, continuing taste changes were observed up to two years post-treatment and likely will continue indefinitely in some patients.

The eating experience is altered leading to patients accommodating with modifications including maladaptation affecting diet and impacting social interactions that influence general well-being and quality of life [18]. In the current study, HNC treatment was associated with patient weight during treatment (less 5% weight loss) and continued during follow up with a mean of 12% loss from pretreatment weight. HNC treatment reduced the pleasure of eating; 66.7% of patients reported unpleasant or very unpleasant taste perception, pain or difficulty swallowing in acute group and in 28.6% of patients with unpleasant or very unpleasant eating in the post treatment group. Therefore, the impact of treatment toxicities affecting diet and nutrition must be assessed during and following HNC treatment. Patients reported reduced ability to eat a full meal, which clearly challenges calorie and nutrient intake. In addition, the time required to consume a meal was increased which has significant implications in the social setting. Appetite decline has significant implications in survivorship and is both understudied and underappreciated. Our results show a considerable and continuing impact of treatment upon appetite during treatment and greater impact following treatment.

A post-treatment survey following HNC treatment found only 28% reported a normal full diet [17]. They identified clinical correlations with T stage, location of primary tumor, combined RT/CT were associated with poor oral intake [17]. Symptoms of dry mouth, difficulty swallowing, mucus secretion, taste and choking/coughing with eating were most impactful [17]. This study, focused on survivors, and likely underestimates the frequency, severity and impact of oropharyngeal function in the broader HNC population. Our study reports similar findings and further evaluated components of oral health and taste and olfaction in addition to general PRO. In addition, our report emphasizes the differences between acute and chronic complications during the cancer journey of HNC patients. Our study shows that oropharyngeal function, taste, flavor, and appetite are complex and multidisciplinary constructs. Diet and nutrition affect health and social well-being and require evaluation across the continuum of oncology care from treatment and throughout survivorship.

Taste perception may have profound impact on health and requires attention of the health care team. While current approaches to nutrition and diet management have emphasized nutritional supplementation, little attention has been paid to oropharyngeal factors that influence comfort, taste and dietary choices and appetite [9]. The current study shows changes in the oral conditions throughout the HNC treatment continuum require management. We assessed saliva function, oral hygiene, gingivitis and mucosal change that may impact oral function and affect diet. Dental status was reported by Kamal et al. [17], may

impact quality of life and oral function. Taste management should include addressing oral status including acute mucosal damage (mucositis), pain management, oral hygiene, and addressing dental/oral disease and saliva management. Current guidance for medical intervention in taste change is based on preliminary studies. [9,32].

Our findings suggest that attention to diet and nutrition must include management of oral conditions and modifications of diet recommendations and food product development. These factors should be considered in diet and nutritional advice and products, seeking high calorie, protein and nutrient content in meals, meal replacements and supplements. Future studies should examine and manage oral health, taste and examine flavor in HNC patients in order to improve patient dietary needs and nutrition.

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DECLARATIONS

Ethics approval and consent to participate: Western Institutional Review Board (WIRB, Puyallup, WA; IRB # 20172768) approved the study and all patients provided written informed consent to participate.

Consent for publication: All authors consent to publication.

Availability of data and material: Data is not publicly available.

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Authors' contributions:

JE: made substantial contributions to the conception and design of the work; responsible for the acquisition, and interpretation of data; have drafted the work or substantively revised it

DV: made substantial contributions to the design of the work; responsible for the analysis and interpretation of data; have drafted the work or substantively revised it

GE: responsible for the acquisition; have drafted the work or substantively revised it

GS: made substantial contributions to the conception and design of the work; have drafted the work or substantively revised it

All authors have approved the submitted version and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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