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Exploratory Research: Patient-Reported Factors Contributing to Decreased Oral Intake During Radiotherapy in Head and Neck Cancer

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ABSTRACT

Background: Radiotherapy (RT) in head and neck cancer (HNC) can cause multiple side effects such as nausea, pain, taste loss, fatigue, oral mucositis, xerostomia, and acute radiation-associated dysphagia (RAD). These factors threaten patients' oral intake (OI) during this RT. Reduced OI can cause weight loss, dehydration, malnutrition, and various comorbidities. On top, reduced OI significantly affects quality of life and may contribute to RAD through the disuse of swallowing muscles. With the aim of maximizing the retention of a patient's OI, it is important to gain an insight into the factors that have the greatest impact. Therefore, this study aims to identify the impact of contributing factors on decreased OI during RT.

Methods: During their treatment, 55 HNC patients completed an OI questionnaire at 5 different time points: during weeks 1, 2, 3, and 4 and at the end of RT (week 7). First, patients rated the OI compared to pre-RT on a 100 mm visual analogue scale (VAS). Subsequently, patients reported on separate VAS the degree to which pain, fatigue, loss of taste, loss of smell, loss of interest in food, nausea, and loss of hunger contributed to the decrease in OI (0: no contribution; 100: complete contribution). SPSS version 27 was used to analyze the results.

Results: OI decreased over time during RT, with the lowest OI at the end of RT. During the first 4 weeks of RT, the impact of all factors with pain, loss of taste, loss of interest in food, and loss of hunger pointed out as strongest contributing factors to a decreased OI. The most important patient-reported impacting factor on OI was loss of taste. At the end of RT, the importance of pain and nausea still increases, while the contribution of the other factors drops slightly.

Conclusion: This cohort study shows that several factors contribute to a decreased OI in HNC patients during RT. This study is the first prospective analysis to identify self-reported factors contributing to reduced OI. Results demonstrate that taste has the greatest impact on OI followed by loss of interest in food, loss of hunger, and pain.

1 | Introduction

Head and neck cancer (HNC) is the collective term for malignant epithelial tumors of the oral cavity, nasal cavity and sinuses, larynx, and pharynx [1]. Depending on subsite and staging, concurrent chemoradiotherapy (CCRT) is now the standard of care for advanced HNC, alongside surgery. CCRT is associated with improved survival compared with either radiotherapy (RT) alone or the sequential application of RT and chemotherapy [2–10].

From the first beam, RT induces an inflammatory process affecting the epidermis, mucosa, and exposed muscle fibers, gradually leading to the development of tissue fibrosis and atrophy [11]. During RT, the inflammatory process leads to so-called acute toxicities such as radiation dermatitis, xerostomia, edema, dysgeusia, taste and muscle deterioration, and mucositis [12–15]. The latter is associated with head and neck pain and discomfort. Typically, the severity of these side effects is more pronounced in CCRT compared to RT alone and increases during the course of RT [16].

The discomfort and pain caused by acute toxicities, combined with fatigue and nausea, often challenge patients' motivation to continue eating during RT/CCRT [11, 17]. On top, reduced oral intake (OI) significantly affects quality of life (QOL). Research by George et al. (2021) shows significant negative associations between OI and all domains of overall QOL. Dysphagia affects all aspects of life, as expressed by reducing individual's dignity, self-esteem, security, work, capacity, exercise, leisure and the regard of others. Results suggest that as OI decreases, the QOL of these individuals deteriorates [18]. These findings are consistent with other studies stating that reduced functional OI leads individuals to avoid socializing with friends and family over time, which in turn increases the level of depression and frustration that affects their mental health [19–23].

Besides the negative impact of reduced OI on QOL, reduced OI may also contribute to radiation-associated dysphagia (RAD) through the disuse of swallowing muscles. RAD is generally considered to be one of the most common and serious side effects of RT, affecting both the safety and efficiency of swallowing. Both RAD and the associated anxiety threaten the patient's OI [11, 15, 24–32].

Reduced OI puts patients at risk for malnutrition and/or dehydration [24, 33]. Malnutrition occurs in more than 50% of HNC patients and has a significant negative impact on QOL [34]. It might also lead to increased mortality, altered metabolic processes, malabsorption and gastric atony [34, 35]. These factors impact treatment outcome, length of hospital stay, the total amount of complications, and prognosis [36, 37].

Moreover, reduced OI also implies reduced number of swallows and resistance to the swallowing mechanics, and may subsequently evoke disuse atrophy and more severe dysphagia leading to increased morbidity and mortality [38]. Hutcheson and colleagues showed that patients engaging in both eating and swallowing exercises during RT/CCRT obtain the highest rate of return to a regular diet. This is in agreement with the "use it or lose it" paradigm. This emphasizes the importance of maintaining maximal OI [17, 29, 38, 39].

Patient perspective can be measured by using patient-reported outcomes (PROs). Understanding the current health state of the patient is useful as it can affect directly their QOL and their ultimate satisfaction with care [40–42]. Although researchers and clinicians are well aware of the impact of acute toxicities and RAD on OI during RT/CCRT in HNC patients, there is limited understanding of the extent to which each of these factors, according to the patient, contributes to OI and how this impact evolves during the course of therapy. Therefore, this study aims to identify the patient-reported factors responsible for reduced OI during RT.

2 | Methodology

The study was approved by the Medical Ethics Committee: Ethics Committee of the Antwerp University Hospital (UZA) with reference B300201835273. Local ethical approval has been obtained from the Ethical Committees of the Ghent University Hospital and Ghent University, Leuven University Hospital and Leuven University, and AZ Sint-Jan Hospital Bruges.

2.1 | Study Design

Data were prospectively collected for secondary analyses of the multicenter PRESTO trial. The main goal of the PRESTO trial was to investigate the difference in adherence and swallowing outcome variables during and after prophylactic swallowing exercises in HNC patients performing the same therapy schedule, receiving different delivery methods (practicing at home, practicing at home with continuous counseling of an app or face to face therapy by a speech and language pathologist). The broad outlines and primary outcome data have already been published [38, 43]. Written informed consent was obtained from all participants and their data were pseudonymized.

2.2 | Participants

Patients with a stage III or IVA-B (TNM7) diagnosed squamous cell carcinoma of the oropharynx were recruited for this study. Patients were eligible if they were over 18 years of age, and had no cognitive or language deficits that could interfere with the correct implementation of the PRESTO prophylactic swallowing therapy protocol. All patients were treated for 6–7 weeks with fractionated RT/CCRT with or without induction chemotherapy. Exclusion criteria were the presence of a recurrent carcinoma or metastasis from a non-HNC carcinoma and previous RT/CCRT or surgery in the head–neck region with possible impact on swallowing function. We decided to include OI data at a later stage of the PRESTO data collection. Therefore, we only have OI data from 55 patients of the 150 HNC patients included in the PRESTO trial. OI data was collected in all groups of the presto trail. The data collection was longitudinal, continuous, and free of selection bias. Only 4 of the 55 included patients

had a preventive percutaneous endoscopic gastrostomy (PEG) (=7.8%).

2.3 | Materials and Methods

A study-specific questionnaire was developed to assess (1) the degree of OI compared to pre-RT and (2) the patient-reported relative contribution of each RT-side effect to the reduction in OI. Participants completed the OI questionnaire at 5 different time points during RT: during weeks 1, 2, 3, and 4 and at the end of RT (Week 7), no data was collected in weeks 5 and 6 of RT treatment.

First, patients were asked to indicate on a visual analogue scale (VAS) whether their OI had decreased compared to before the start of RT. When patients indicated a decrease in OI, they were asked to continue the questionnaire and report the degree to which pain, fatigue, loss of taste, loss of smell, loss of interest in food, nausea, and loss of hunger contributed to this by means of a vertical mark on a factor specific 100 mm-VAS per factor (0: no impact; 100: complete impact). The distance to the vertical mark was then measured to create a score.

2.4 | Statistical Analysis

Medians and interquartile ranges of VAS scores were calculated. Boxplots were used to visualize the evolution of the OI over time.

The evolution was further studied using the Friedman test for repeated measures, followed by pairwise comparisons versus baseline with Wilcoxon signed rank tests. Bonferroni correction was applied to correct for multiple testing.

Formal statistical comparisons for the relative contribution per factor over time during RT could not be performed as no information on factors was available for the patients with stable OI.

All analyses were performed by means of IBM SPSS v27 (IBM, Armonk, New York).

3 | Results

3.1 | Participants

Patients, disease and treatment characteristics can be found in Table 1.

3.2 | The Evolution of the OI Over Time During RT

The mean patient-reported OI in week 1 was still approximately 95% compared to the pre-RT OI (Figure 1). At week 2, the mean OI decreased to 70%, with a further decrease to 50% at week 3, 30% at week 4 and 25% at week 7 ($p < 0.001$). Accordingly, patient-reported OI in this study was lowest at the end of treatment (week 7).

TABLE 1 | Patients, disease, and treatment characteristics.

Age	*M*	62.42
	SD	9.46
	Range	45
Gender	Male	42
	Female	13
T classification	1–2	31
	3–4	24
N classification	0	5
	1	7
	2–3	43
Treatment	RT	9
	CRT	46
HPV status	Positive	24
	Negative	31
Preventive PEG	Yes	4
	No	51

Abbreviations: CRT chemoradiotherapy; M, mean, RT radiotherapy, SD standard deviation.

3.3 | The Relative Contribution per Factor Over Time During RT

The bar chart in Figure 2 shows the contribution of each factor over time expressed by the mean VAS score. Table 2 shows the number (*N*), the median (*M*), the interquartile range (Q-range), and the minimum and maximum per factor over time. During the first 4 weeks of RT, the contribution of all factors increases, with pain, taste, loss of interest in food, and loss of hunger reported as the most important. The most important reported factor impacting the OI was loss of taste. At the end of RT, the importance of pain and nausea increased even more, while the contribution of the other factors had already decreased slightly. Individual differences should be taken into account while interpretating the results.

4 | Discussion

Adequate nutrition during RT in HNC patients is essential to avoid malnutrition, comorbidities, and mortality [24, 33–37]. Additionally, there is international recognition of the significance of continued OI for maximum prevention of both acute and chronic RAD [38, 39]. However, continuing OI during RT is impeded by the RT-induced acute toxicities. To date, our understanding of the factors contributing to a decreased OI, and the extent to which these factors influence the OI remains limited.

This study is the first study providing patient-reported data giving deeper insight into the extent to which various acute toxicities might affect OI. Results demonstrate that -of the questioned contributing factors-taste, lack of interest in food, lack of hunger and pain have the greatest impact on OI during RT in HNC, with taste being the most impacting factor.

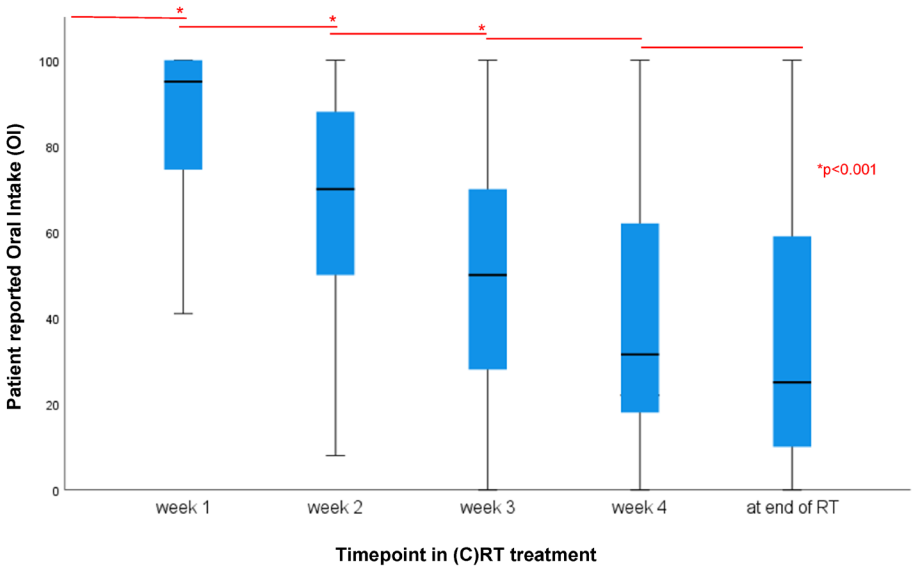
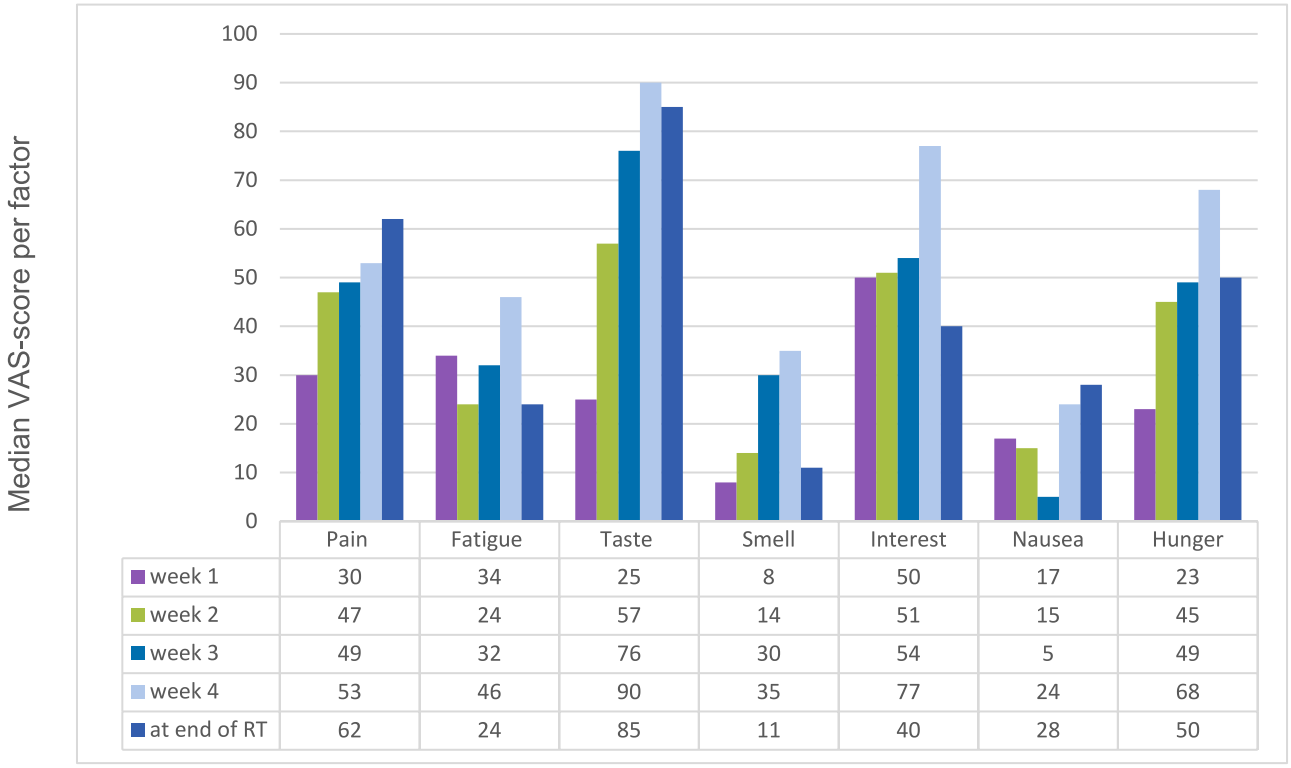


FIGURE 1 | Box plots presenting the evolution of the median VAS scores of the patient-reported oral intake over time in patients treated with RT for HNC ($n = 55$); The plot shows the median (black line), the interquartile range Q1 and Q3 (blue box), and the minimum and maximum values (whiskers). [Color figure can be viewed at wileyonlinelibrary.com]



	Pain	Fatigue	Taste	Smell	Interest	Nausea	Hunger
week 1	30	34	25	8	50	17	23
week 2	47	24	57	14	51	15	45
week 3	49	32	76	30	54	5	49
week 4	53	46	90	35	77	24	68
at end of RT	62	24	85	11	40	28	50

FIGURE 2 | The evolution of the median of the VAS score per factor over time in patients treated with RT for HNC ($n = 55$). [Color figure can be viewed at wileyonlinelibrary.com]

In order to maximize OI during RT and prevent RAD, it is appropriate to manage the impact of the patient-reported factors as accurately as possible. Taste, interest, hunger, and pain deserve heightened attention. However, the contribution of other influencing factors should not be underestimated either, and individual differences should be taken into account. The wide interpatient variation highlights the importance of a systematic, patient-centered approach to controlling and managing these influencing factors. This poses a significant challenge to healthcare professionals.

Several studies indicate the importance of preventive education when it comes to *loss of interest in food* and *loss of sense of hunger* [44, 45]. Education of the patient regarding the side effects and difficulties during the treatment process as well as the importance of continuing to eat despite these difficulties is necessary.

TABLE 2 | Number (*N*), Median, Interquartile range (Q-range), and range (min-max) of VAS scores per factor over time.

		N				
Timepoint	**Factor**	**Valid**	**Missing**	**Median**	**Q-range**	**MIN – MAX**
Week 1	Pain	25	30	30	48	0–85
	Fatigue	25	30	34	60	0–90
	Taste	25	30	25	62	0–100
	Smell	25	30	8	47	0–92
	Interest	25	30	50	50	0–76
	Nausea	25	30	17	67	0–94
	Hunger	25	30	23	55	0–76
Week 2	Pain	30	24	47	54	0–85
	Fatigue	29	25	24	49	0–100
	Taste	30	24	57	63	0–100
	Smell	29	25	14	29	0–86
	Interest	30	24	51	61	0–92
	Nausea	30	24	15	50	0–92
	Hunger	30	24	45	64	0–90
Week 3	Pain	38	16	49	62	0–98
	Fatigue	38	16	32	55	0–85
	Taste	38	16	76	53	0–100
	Smell	37	17	30	66	0–100
	Interest	37	17	54	47	0–97
	Nausea	38	16	5	51	0–93
	Hunger	38	16	49	57	0–100
Week 4	Pain	38	16	53	48	0–100
	Fatigue	38	16	46	69	0–92
	Taste	37	17	90	26	5–100
	Smell	37	17	35	67	0–100
	Interest	38	16	77	44	0–100
	Nausea	39	15	24	61	0–100
	Hunger	39	15	68	60	0–100
At end of RT	Pain	31	19	62	46	0–100
	Fatigue	30	20	48	57	0–93
	Taste	31	19	85	57	8–100
	Smell	29	21	11	67	0–98
	Interest	30	20	40	72	0–92
	Nausea	30	20	28	65	0–94
	Hunger	31	19	50	63	0–100

Regarding treatment options for pain and loss of taste, more concrete options are available For *pain*, the WHO indicates that one should start pain medication in a timely manner [46]. Pain medication should be built up starting with non-opioids, mild opioids, and only in a third step strong opioids. Medication should not be administered on demand but around the clock.

One can use both local and systemic pain control. To specifically treat mucositis-induced pain, there is evidence for the mouthwash protocol [47].

Finally, dieticians play an important role in the treatment of *taste*. They can provide dietary advice to enable the patient to keep eating and enjoying food, given the changes in taste [48]. Based on recent literature, a possibility is taste-controlled food or meals. Corremans M. et al. (2021) developed a self-care intervention based on taste control. This intervention contains an assessment of the individual taste and food hedonics. It provides recipes based on the individual assessed hedonics profile, so patients can self-prepare personalized meals [49].

The multidisciplinary oncology team recognizes the critical need to manage acute toxicities from radiation therapy (RT), as they significantly affect patients' OI and overall QOL [50, 51]. Effective monitoring and assessment of OI are vital components of this approach. Key strategies include:

1. OI assessment: Regular evaluations using instruments like the Functional Oral Intake Scale (FOIS) [52] and Food Intake Level Scale (FILS) [53] help measure OI severity. Dietitian expertise is crucial for determining caloric intake, and informing decisions about enteral feeding when intake is insufficient.
2. Identifying influencing factors: It is vital to pinpoint factors reducing OI. Upon further validation, the study-specific questionnaire can be used. Alternatively, pertinent information can be extracted from existing, validated tools. Table 3 provides an overview of instruments that can be used to measure the impact of pain, loss of interest, loss of taste, and loss of hunger on OI.

A comprehensive monitoring policy that incorporates these strategies will enhance patient care and treatment adherence, ultimately improving outcomes in oncology.

TABLE 3 | Overview of valid tools to measure the impact of pain, loss of interest, loss of taste, and loss of hunger on OI during RT.

Pain	– Eating Assessment Tool –10 (EAT-10) [54]. A self-report questionnaire for patients consisting of 10 items. It serves as a subjective assessment encompassing the patient's perception regarding their inability to perform certain activities. – Oral Mucositis Weekly Questionnaire Head and Neck cancer (OMWQ-HN) [55]: A validated, reliable, and easily manageable patient questionnaire that explores the symptoms of mucositis, oral and throat discomfort, and their impact on the patient's well-being and functionality. – MD Anderson Symptom Inventory—Head & Neck (MDASI-HN) [56]. The MD Anderson Symptom Inventory (MDASI) is a multi-symptom patient-reported outcome (PRO) measure for clinical and research use. The MDASI can be used to assess the severity of symptoms experienced by patients with cancer and the interference with daily living caused by these symptoms. The MDASI–HN is a specific MDASI questionnaire for head and neck cancer patients. Along with the core MDASI's 13 symptom items and 6 interference items, the MDASI–HN also specifically assesses 9 symptoms relevant to head and neck cancer.
Interest	– EAT-10 [54]
Taste	– Mann Assessment of Swallowing Ability-Cancer (MASA-C) [57]. The inquiry seeks a comparison of taste perception before cancer treatment with taste perception at the time of testing. Response options range from: diminished taste, no taste, to normal taste. – MDASI—HN [56].
Hunger	– Mini Nutrition Assessment (MNA) [58]. The inquiry pertains to whether the patient has reduced their food intake due to decreased appetite. Answer options range from a significantly reduced appetite (score of 0), to a score of 2 for no reduced appetite, and a score of 1 indicating a moderately reduced appetite. – MDASI—HN [41].

4.1 | Limitations

Results of this research must be interpreted with the understanding that no OI data were collected in weeks 5 and 6 of RT treatment. In this study, self-reported OI is lowest in week 7. However, data from weeks 5 and 6 are missing. It is possible that OI during these weeks is even lower than the OI reported in week 7, as the toxicities of RT tend to peak during this time [59, 60]. Second, the list of possible influencing factors is not exhaustive. Several other factors may influence OI. Since in our population only 4 participants received a preventive PEG, we have no significant data or insights regarding the effect of prophylactic PEG on OI. Furthermore, this study involved a relatively small number of participants [61]. Conducting repeated research on a larger population is recommended to confirm the findings. Another limitation that should be mentioned is the relatively high number of missing data at several time points.

There has been an increasing emphasis on 'quality' in health care over the last 15 years. As a result, next to the relatively traditional and narrow conceptualization of quality equating it primarily with safety and effectiveness, the term quality actually encompasses a much broader scope, importantly including the patient experience/perspective with care [41]. The patient's perspective is multidimensional, and has been measured through the use of PROs [42]. The US Federal Drug Association defined PROs as any report of a patient's health status that comes directly from the patient, and can measure patient symptoms, patient function, and QOL [62]. Understanding the current health state of the patient is useful because it can affect directly their QOL and their ultimate satisfaction with care [40–42]. Moreover, a study by Nund et al. (2014) found a discrepancy between purely clinical assessments and findings reported by patients using PROs. This

shows that clinician-rated instruments and PROs measure different health-related domains [63]. Accordingly this highlights the importance of eliciting the patient perspective. Given the importance of the patient perspective, only PROs were collected to answer the research question. No additional objective measures as patient and food weight or caloric intake were made.

5 | Conclusion

Several factors can contribute to a decreased OI in patients during RT. It is essential to identify all those factors for healthcare professionals to anticipate accurately and improve patient-centered care. This study is the first prospective analysis to identify self-reported factors contributing to a lower OI. Results indicate that loss of taste, loss of food interest, loss of hunger, and pain have the greatest impact on a decreased OI within the HNC population, with loss of taste having the highest impact.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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