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Original Article

A pilot study of quality of life domains before and after radiotherapy in patients with head and neck cancer

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ABSTRACT

Purpose: The aim of the study was to examine the worsening of QoL in patients with HNC before and after cancer therapy and to assess the extent that each factor has in its worsening.
Methods: A prospective study was developed to analyze the QoL of patients with HNC before and after curative radiotherapy. The patients were interviewed to assess QoL within 15 days after initiation and at least 15 days after completion of radiotherapy. QoL assessment was performed by University of Washington Quality of Life Questionnaire version 4.1.
Results: The questionnaire before and after radiotherapy was completed by 22 patients. "Fear of recurrence" was the main important domain pre- and post-radiotherapy. Regarding the global questions we noticed a lower percentage of patients who rated positively their QoL from before to after radiotherapy. It was possible to note that there were statistically significant differences for "taste" ($p=0.018$) and "saliva" ($p<0.001$). The comparison between Physical Function and Social-Emotional Function before and after radiotherapy showed that there was a statistically significant difference in QoL related to Physical Function, which worsens after radiotherapy.
Conclusion: This pilot study showed that fear of recurrence is the most important domain for HNC patients undergoing radiation therapy, followed by saliva, taste and swallowing.

Introduction

Worldwide, head and neck cancers (HNCs) are widespread (650,000 cases per year) and cause more than 330,000 deaths per year. Almost all cases, about 90%, are cancers of the oral cavity, oropharynx, and larynx [1]. In conventional clinical practice, HNCs are treated primarily with surgery, often used in combination with radiation therapy (RT) and/or chemotherapy [2]. Like most anti-neoplastic therapies, RT carries significant adverse effects both acute and chronic. Both types of adverse effects have a significant impact on quality of life (QoL) [3].

HNC patients attach great importance to their health-related quality of life [4]. In addition, there is evidence that the QoL of HNC survivors is poorer than that of the general population due to the significant functional limitations caused by the disease and treatment [5], this is because the head and neck district is the site of several organs that play an important role in the basic functions of daily life, including breathing, speeching, chewing, and swallowing, and are important for appearance. Moreover, HNC leads to a high incidence of psychosocial problems among survivors, such as depression, social isolation, and addiction and substance abuse, which in turn post to negative consequences regarding QoL [6].

QoL is often used as an outcome to assess the efficacy and safety of cancer treatment, both during short and long follow-ups [7–9]. In this context, patients with head and neck cancers were classified as short-term survivors (follow-up period minor to 1 year after cure), mid-term survivors (follow-up period between 1 and 3 years after cure) or long-term survivors (follow-up period beyond 3 years after cure) [10]. A tool capable of identifying which aspects of QoL undergo the greatest changes due to cancer therapy would be most useful to identify the interventions that are likely to slow or prevent functional deterioration in patients with HNC.

Several questionnaires subjectively assessing QoL have been proposed in the literature, the most widely used being the EORTC, the FACT and the UW-QOL. However, the UW-QOL v4 is a validated questionnaire specifically for patients with HNC, which considers the patient's general well-being and allows for the identification of subtle changes by

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ascertaining which aspect of quality of life changes the most [11]. The aim of this study is to examine the change of QoL in patients with HNC prior to the initiation of radiotherapy (up to 15 days) and after cancer therapy and to assess the extent that each factor has in its change.

Materials and methods

A prospective study was developed to analyze the QoL of patients with HNC before and after curative radiotherapy. The protocol was approved by the Ethics Committee of the A.O.U. Città della Salute e della Scienza of Turin by protocol number 000030 dated 07/01/2025 and was registered on ClinicalTrial.com (NCT06807697 – 29 January 2025).

The present study was conducted in the Department of Prosthesis and Maxillo-Facial Rehabilitation, C.I.R. Dental School in Turin, A.O.U. Città della Salute e della Scienza of Turin in accordance with the Declaration of Helsinki and its later amendments.

We used an opportunistic convenience sample for this prospective study. All patients were included in the study, after authorization by informed consent, from January 2025 to April 2025.

The sample was selected through the following inclusion criteria:

- patients with HNC and waiting to undergo curative radiotherapy or, if previously operated, adjuvant radiotherapy;
- patients between the ages of 18 and 75 years;
- patients who presented at their first dental visit with a diagnosis of HNC.

They were excluded from the study:

- patients who had already undergone cancer therapies (excisional surgery or chemotherapy or radiation therapy) at the time of the first dental visit;
- patients with an indication for palliative or symptomcontrol radiotherapy;
- patients with depression or social anxiety;
- patients with language difficulties.

The investigator visited the first patients sent by the radiotherapy department of the A.O.U. Città della Salute e della Scienza of Turin daily and enrolled them in the study. After obtaining written consent, patients underwent a dental examination and variables related to caries experience (Decayed Missed Filled Teeth) and periodontal history (Pocket Depth; Full Mouth Plaque Score; Full Mouth Bleeding Score) were collected. Subsequently, they were interviewed to assess their quality of life within 15 days of starting and at least 15 days after completing radiotherapy.

QoL assessment was performed by University of Washington Quality of Life Questionnaire version 4.1 (UW-QOL V4.1), developed by Lowe and Rogers [12]. The UW-QOL v4.1 is a widely recognized questionnaire for reporting physical and socio-emotional dysfunction after HNC treatment [13] and consists of short multifactorial questions specific to HNC and to assess the patient's perception of general QoL in the past 7 days. The questionnaire includes 12 questions to assess pain, appearance, activity, leisure, swallowing, chewing, speech, shoulder, taste, salivation, mood, and anxiety. There are two subdomains: physical and social-emotional. The physical function items are chewing, speech, swallowing, taste, saliva and appearance. Social function includes anxiety, mood, pain, activity, recreation, and shoulder function.

In addition, The UW-QOL v4.1 proposes some general questions and allows the respondent to choose the 3 factors that the patient considers most important. General questions investigate patients' condition before developing cancer, (b) on their health-related QOL, and (c) on their overall QOL. The worst possible answer is represented by “0,” while the best possible answer is “100”. Intermediate scores, which may or may not be available for each domain, are 0, 25, 30, 40, 50, 60, 75, 80 and indicate the level of the response between worst and best. Because of the intimate and personal nature of some of the questions, the UW-QOL was filled out by the patient in the waiting room so that the subject could be free to answer without having to speak aloud.

Statistical analysis

The collected data were stored in s Microsoft Excel spreadsheet (version 14.4.9) and then processed with Jamovi (version 2.3.28.0). The results were presented according to the UW-QOL V4.1 guidance for scoring and presentation by Lowe and Rogers (update 21 January 2018). Qualitative data were reported as percentages, whereas mean ± standard deviation was reported for quantitative variables. To test whether the distribution of the data was normal, the Shapiro-Wilk test was used. Student's t test for paired data was used to compare data before and after radiation therapy for parametric data. Pre- and post-Cronbach alpha reliability coefficient was used, $p < 0.05$ was considered as significant.

Results

An opportunistic convenience sample of 39 patients was recruited, of these 17 patients were not evaluated after radiotherapy: 2 patients did not agree to fill out the questionnaire again; 5 patients died during therapy due to disease progression; and 10 patients did not show up for follow-up (Fig. 1). The 22 patients included in the study (Table 1), were 8 females and 14 males with a mean age of 61.4 years (SD 9.5 years). 7 patients (31.8%) reported being smokers at the first visit. The study population was heterogeneous in terms of tumor characteristics and treatment modalities. Primary tumor site varied, with the oral cavity being the most common location (31.8%), followed by the nasopharynx and oropharynx (both 18.2%), tongue (13.6%), and less common sites, including unknown primary tumors. Disease stage distribution was skewed toward advanced disease, with nearly half of patients presenting with stage III–IV tumors (45.4%), while early-stage disease (stage 0–II) accounted for the remainder. Regarding treatment modality, most patients underwent multimodality therapy, with combined radiotherapy and concomitant chemotherapy being the most common approach (45.5%), followed by trimodality treatment including surgery (27.3%) and radiotherapy combined with surgery alone (22.7%), while radiotherapy alone was rarely administered (4.5%). Although functional status was not formally quantified using standardized scales, all patients had a relatively preserved baseline functional status. The characteristics of the sample are summarized in Table 1.

DMFT: Decayed Missed Filled Teeth; FMPS: Full Mouth Plaque Score; FMBS: Full Mouth Bleeding Score; PD: Pocket Depth; RT: Radiotherapy; CCT: Concomitant chemotherapy; EX: Surgical intervention.

At baseline, QoL scores were generally high across most domains of the UW-QOL questionnaire. The highest mean scores were observed for speech (89.09), saliva (89.55), and swallowing (86.82), indicating relatively preserved physical function before treatment. In contrast, lower scores were reported for mood (72.73) and anxiety (71.36), suggesting a relevant psychological burden already present before radiotherapy.

After radiotherapy, a general decline in several QoL domains was observed, particularly in physical functions. The most pronounced reductions in mean scores were noted for taste (from 77.73 to 55.45) and saliva (from 89.55 to 59.55).

Other domains such as swallowing and chewing also showed worsening trends, although less marked. In contrast, some domains, including pain and shoulder function, showed stable or slightly improved scores.

The results of questionnaires completed by patients before and after radiation therapy were listed and summarized along with the mean scores followed by the percentage of patients with the best possible score 100 (Tables 2 and 3). Shaded boxes contain values that do not exist for that domain.

Responses regarding the importance assigned by the patient to the

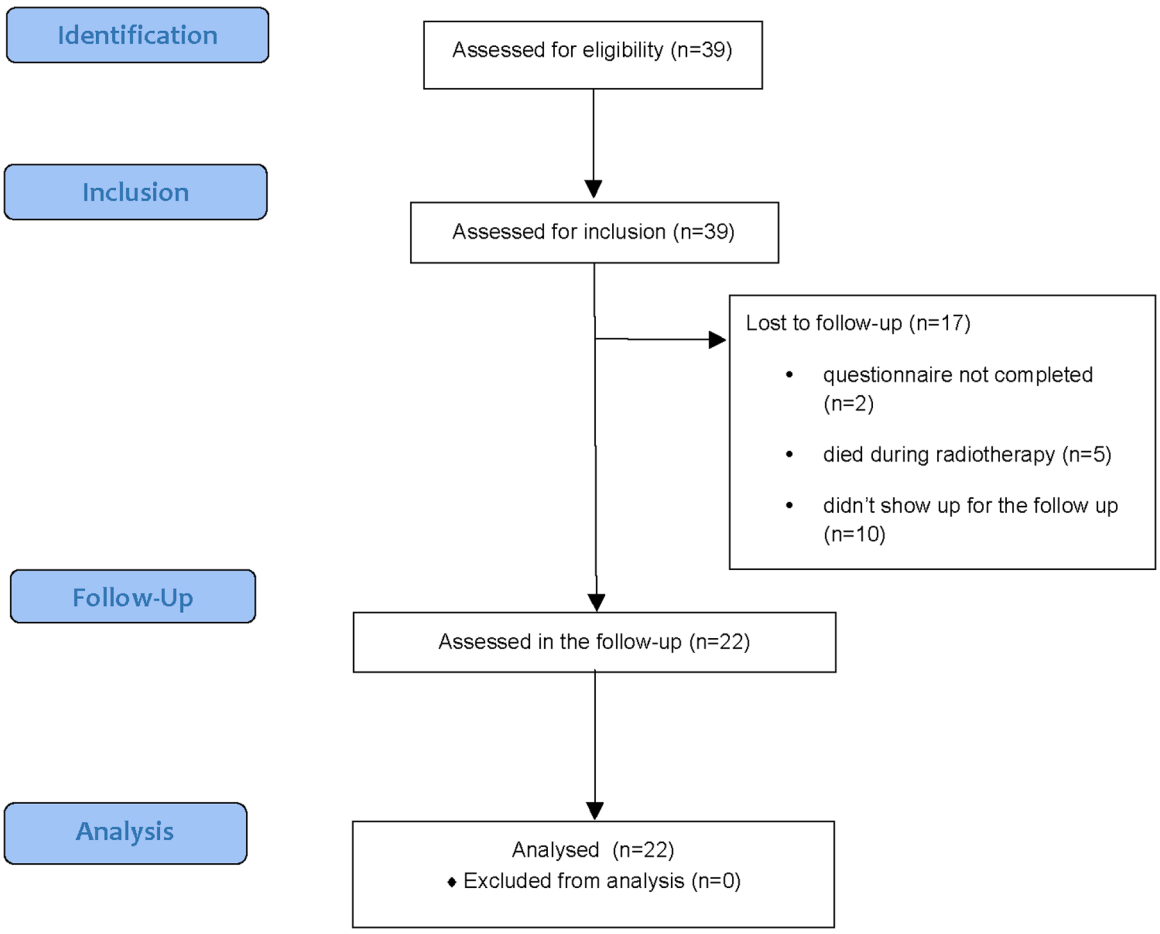

Fig. 1. Flowchart detailing patient inclusion and losses.

various domains were ranked from highest to lowest priority. Regarding the pre-radiotherapy assessment, 10 patients (45.45%) have chosen "fear of recurrence" as the most important domain, followed by "activity" and "anxiety" both chosen by 6 patients (27.27%). The domains "taste," "speech" and "pain" were the least chosen by patients (4.55%).

In the post-radiotherapy evaluation, "fear of recurrence" remained the most popular topic (63.64%), followed by "activity," chosen by 12 patients (54.55%), and "anxiety" indicated by 8 patients (36.36%). No one indicated "taste" as the most important topic.

Table 4 summarizes the responses inherent in the importance the patient places on the various domains.

The comparison between baseline and post-treatment scores revealed statistically significant differences in specific domains. In particular, "taste" ($p = 0.018$) and "saliva" ($p < 0.001$) showed a significant deterioration after radiotherapy.

Other domains, such as swallowing, approached statistical significance ($p = 0.052$), suggesting a clinically relevant worsening that may not have reached significance due to the limited sample size.

For most of the remaining domains, no statistically significant differences were observed (Table 5).

When QoL domains were grouped into Physical Function and Social-Emotional Function, distinct patterns emerged.

Physical Function showed a statistically significant decline after radiotherapy, with mean scores decreasing from 83.3 (SD 14.3) at baseline to 70.8 (SD 12.7) post-treatment ($p < 0.001$).

Conversely, Social-Emotional Function did not show significant changes over time, with mean scores of 75.6 (SD 17.9) before treatment and 78.6 (SD 12.9) after treatment ($p = 0.437$).

The responses were clustered into Physical Function and Social-Emotional Function. The comparison between the two cluster before and after radiotherapy is shown in Table 6.

Discussion

The aim of the present study was to evaluate the worsening of QoL in patients with HNC undergoing radiotherapy and the weight of specific factors that may adversely affect the patient's QoL. For QoL assessment, the UW-QOL v4.1 was used, which allows the reporting of physical and socio-emotional dysfunction in patients undergoing cancer therapy [13] and multifactorally assesses HNC-specific QoL components while also providing an overall QoL assessment of the patient.

Head and neck cancer (HNC) is the seventh most common cancer in the world [14]. The diagnosis and treatment of HNC are traumatic events in patient's life, and often, many HNC patients live with worry and uncertainty [15]. It has been shown that psychological distress is common after receiving a diagnosis of HNC and that such distress interferes with QoL [16]. Patients with HNC manifest anxiety, depression, worry about the future [17]. In addition, the diagnosis of HNC could have many functional or social consequences such as increased sensitivity to pain, dysgeusia, while difficulties in daily life include financial difficulties and difficulties resulting from low social support [16].

The present study showed that fear of recurrence is the main factor that determines the QoL of patients with HNC. Fear of recurrence is, in turn, influenced by psychological factors, but mainly by physical factors such as pain and fatigue [18]. In addition to fear of recurrence, patients interviewed before radiotherapy reported "activity" and "anxiety" as the main factors. In the post-radiotherapy evaluation, in addition to fear of recurrence, the main factors were "taste" and "saliva".

Table 1
Characteristics of the sample of HNC patients.

	Overall=22
Age	
Mean (SD)	61.4 (9.5)
Range	38.0-78.0
Gender	
Female	8 (36.4%)
Male	14 (63.6%)
Smoke	
No	15 (68.2%)
Yes	7 (31.8%)
N° Teeth	
Mean (SD)	21.3 (5.86)
Range	9.0-31.0
DMFT	
Mean (SD)	16.8 (5.59)
Range	6.0-28.0
FMPS	
Mean (SD)	57.6 (29.5)
Range	11.3-100
FMBS	
Mean (SD)	36.2 (19.4)
Range	10.0-67.0
PPD	
Mean (SD)	2.85 (0.55)
Range	2.10-3.70
Site of cancer	
oral cavity	7 (31.8%)
Nasopharynx	4 (18.2%)
Oropharynx	4 (18.2%)
Tongue	3 (13.6%)
unknown primary	2 (9.1%)
Other	2 (9.1%)
Stage of cancer	
0	2 (9.1%)
I	4 (18.2%)
II	6 (27.3%)
III	3 (13.6%)
IV	7 (31.8%)
Treatment	
RT	1 (4.5%)
RT+CCT	10 (45.5%)
RT+CCT+EX	6 (27.3%)
RT+EX	5 (22.7%)
Radiotherapy dose	
60 Gy	2 (9.1%)
66 Gy	2 (9.1%)
70Gy	18 (81.8%)

These data are consistent with other studies showing that dry mouth has a negative impact on the QoL of HNC survivors [19]. The issues related to dry mouth, salivary changes, and swallowing disorders after radiotherapy are widely documented [20]. Loss of taste is estimated to affect 50%-75% of patients radiotreated in the head-neck district [21]. Moreover, the study by Martinez et al [22] highlighted dental issues, which may increase pain and further worsen patients' QoL. All these effects could lead to poor patient nutrition and weight loss, which, in addition to contributing to worsening QoL, could compromise the patient's long-term survival [23].

No significant association was observed between smoking status, tumor stage (early vs advanced) or tumor site and QoL changes; however, the study was not powered for subgroup analyses.

According to the present study, many authors have pointed out that the physical component score worsens after radiotherapy, unlike the social-emotional component score, which remains stable [24,25]. The same authors explain that while the Social-Emotional component remained almost unchanged even 2 years after the end of radiotherapy, the physical component recovered as time passes. In this context, the onset of dental and periodontal diseases plays a key role in determining the level of physical QoL [26,27]. It has been estimated that, at the onset of one more symptom, the patient with HNC has a 38.1% chance of having a lower QoL [28] and it has been shown that low levels of QoL could decrease the survival of the patient with HNC [29].

With time, after radiation therapy, independently of the partial recovery of oral function, QoL remains low, suggesting that to improve the QoL of HNC survivors, it may be not sufficient to act on post-treatment rehabilitation, but it seems preferably to intervene preventively interviewing the patients before radiotherapy, taking into account their social and psychological conditions [30].

A recent review [9] summarized the literature on interventions to improve the QOL of patients with HNC. Regarding oral care interventions, the review included 5 studies, supporting that oral hygiene programmes performed post-radiotherapy showed no significant differences in QOL between groups, while, whether oral hygiene protocols were implemented by nutritional assessments, post therapy QoL improved.

The present study adopted an opportunistic sampling strategy rather than a strictly consecutive one. This choice was mainly driven by the clinical setting and the logistical constraints of patient recruitment. Specifically, patients were enrolled during their first dental evaluation within a limited time window prior to the initiation of radiotherapy, and inclusion depended on patient availability, clinical conditions, and willingness to participate. In this context, a fully consecutive sampling approach—requiring the systematic inclusion of all eligible patients—was not feasible.

A significant methodological limitation of the current study is the high dropout rate observed between baseline and post-radiotherapy assessments (17 of 39 patients, or 43.6%). This dropout was primarily due to death during treatment, loss to follow-up, and refusal to complete the second questionnaire. Such a high percentage of missing data may have introduced a survival (or dropout) bias, as the final analysis included only patients who were able to complete radiotherapy and participate in follow-up. Although the baseline characteristics of the excluded patients were comparable to those of the patients included in

Table 2
UW-QOL response before radiotherapy.

UW-QOL	N	0	25	UW-QOL scores 30	50	70	75	100	Mean (SD)	%Best Score (of 100)
Pain	22	0	1		2		8	11	82.95 (20.97)	50.00
Appearance	22	0	2		1		10	9	79.55 (22.67)	40.91
Activity	22	0	0		7		7	8	76.14 (21.10)	36.36
Recreation	22	0	3		3		5	11	77.27 (27.72)	50.00
Swallowing	22	1		1		4		16	86.82 (26.44)	72.73
Chewing	22	2		5		15	79.55 (33.31)	68.18		
Speech	22	0		0		8		14	89.09 (14.77)	63.64
Shoulder	22	2		2		6		12	76.36 (33.03)	54.55
Taste	22	1		3		6		12	77.73 (30.23)	54.55
Saliva	22	0		2		3		17	89.55 (21.93)	77.27
Mood	22	1	1		4		9	7	72.73 (26.62)	31.82
Anxiety	22	2		4		5		11	71.36 (35.23)	50.00
Intimacy	22	1		1		1		19	90.91 (25.80)	86.36
Fear of recurrence	22	2	0		4		7	9	73.86 (30.35)	40.91

Table 3
UW-QOL response post radiotherapy.

UW-QOL	N	0	25	UW-QOL scores 30	50	70	75	100	Mean (SD)	% Best Score (of 100)
Pain	22	0	0		3		5	14	87.50 (18.50)	63.64
Appearance	22	0	0		6		7	9	78.41 (20.84)	40.91
Activity	22	0	0		9		10	3	68.18 (17.56)	13.64
Recreation	22	0	0		8		4	10	77.27 (23.03)	45.45
Swallowing	22	1		1		13		7	74.55 (24.25)	31.82
Chewing	22	1		10		11	72.73 (29.79)	50.00		
Speech	22	0		1		8		13	89.91 (19.19)	59.09
Shoulder	22	0		2		3		17	89.55 (21.93)	77.27
Taste	22	4		4		10		4	55.45 (34.47)	18.18
Saliva	22	0		8		11		3	59.55 (24.97)	13.64
Mood	22	0	3		3		10	6	71.59 (24.76)	27.27
Anxiety	22	0		1		12		9	80.45 (18.64)	40.91
Intimacy	22	0		0		4		18	94.55 (11.84)	81.82
Fear of recurrence	22	3	0		4		12	3	63.64 (29.61)	13.64

Table 4
Importance of conditions before and after radiotherapy.

UW-QOL		Before radiotherapy			After radiotherapy		
	N of response	Patients choosing the domain	% of patients choosing the domain	Rank order	Patients choosing the domain	% of patients choosing the domain	Rank order
Fear of recurrence	22	10	45.45	1	14	63.64	1
Activity	22	6	27.27	2	12	54.55	2
Anxiety	22	6	27.27	2	8	36.36	3
Chewing	22	5	22.73	3	5	22.73	4
Mood	22	5	22.73	6	4	18.18	5
Swallowing	22	4	18.18	4	3	13.64	6
Recreation	22	4	18.18	4	3	13.64	6
Saliva	22	2	9.09	5	3	13.64	6
Shoulder	22	2	9.09	5	2	9.09	7
Intimacy	22	2	9.09	4	2	9.09	7
Appearance	22	2	9.09	5	1	4.55	8
Speech	22	1	4.55	6	1	4.55	8
Pain	22	1	4.55	6	1	4.55	8
Taste	22	1	4.55	6	0	0	9

Table 5
Comparison of domain variation before and post radiotherapy.

UW-QOL	Clinical stage	N	% with best response		% scoring between the two extremes		% with significant problem		p value
Pain	Before	22	**50%**	11	**50%**	11	**5%**	3	0.406
	Post	22	**64%**	14	**36%**	8	**3%**	3	
Appearance	Before	22	**41%**	9	**59%**	13	**6%**	4	0.825
	Post	22	**41%**	9	**59%**	13	**10%**	9	
Activity	Before	22	**36%**	8	**64%**	14	**15%**	10	0.110
	Post	22	**14%**	3	**86%**	19	**11%**	10	
Recreation	Before	22	**50%**	11	**50%**	11	**11%**	7	1.000
	Post	22	**45%**	10	**55%**	12	**10%**	9	
Swallowing	Before	22	**73%**	16	**23%**	5	**3%**	2	0.052
	Post	22	**32%**	7	**64%**	14	**2%**	2	
Chewing	Before	22	**68%**	15	**23%**	5	**3%**	2	0.325
	Post	22	**50%**	11	**45%**	10	**1%**	1	
Speech	Before	22	**64%**	14	**36%**	8	**1%**	1	0.382
	Post	22	**59%**	13	**41%**	9	**1%**	1	
Shoulder	Before	22	**55%**	12	**36%**	8	**6%**	4	0.095
	Post	22	**77%**	17	**18%**	4	**3%**	3	
Taste	Before	22	**55%**	12	**41%**	9	**6%**	4	0.018*
	Post	22	**18%**	4	**64%**	14	**18%**	16	
Saliva	Before	22	**77%**	17	**23%**	5	**5%**	5	<0.001*
	Post	22	**14%**	3	**86%**	19	**12%**	11	
Mood	Before	22	**32%**	7	**64%**	14	**11%**	7	0.847
	Post	22	**27%**	6	**73%**	16	**9%**	8	
Anxiety	Before	22	**50%**	11	**41%**	9	**9%**	6	0.188
	Post	22	**41%**	9	**55%**	12	**1%**	1	
Intimacy	Before	22	**86%**	19	**9%**	2	**3%**	2	0.502
	Post	22	**82%**	18	**18%**	4	**1%**	1	
Fear of recurrence	Before	22	**41%**	9	**50%**	11	**17%**	11	0.071
	Post	22	**14%**	4	**73%**	16	**16%**	14	

Table 6
Variation of Physical Function and Social-Emotional Function before and post radiotherapy.

	Timestep	N	Average	Median	SD	SE	p
Physical Function	T0	22	83.3	86.5	14.3	3.05	
	T1	22	70.8	73.0	12.7	2.70	<0.001*
Social-Emotional Function	T0	22	75.6	82.0	17.9	3.82	
	T1	22	78.6	79.0	12.9	2.76	0.437

the final analysis, individuals with worse clinical conditions or more severe treatment-related toxicity—who are also more likely to experience a greater deterioration in quality of life—may have been underrepresented in the post-treatment assessment. This may have led to an underestimation of the true negative impact of radiotherapy on quality of life outcomes. Therefore, the results should be interpreted with caution, as they may reflect a relatively healthier subgroup of the original cohort rather than the entire population of head and neck cancer patients undergoing radiotherapy. Future studies with larger samples and strategies to minimize losses to follow-up are needed to better address this potential source of bias.

No formal sample size calculation was performed, as this study was designed as an exploratory pilot analysis. Therefore, the sample size limits the ability to identify real differences before and after treatment, as it cannot be considered fully representative of the head and neck cancer patient population, lending the results a more exploratory nature.

In this study, QoL was assessed using the UW-QOL questionnaire, which was chosen for its feasibility and specificity. However, the use of more comprehensive instruments such as the EORTC QLQ-C30 combined with the HN35 module could provide a more detailed assessment and improve comparability between studies.

In a context of limited resources for the care of patients with HNC, preventive care should be promoted, so that the decrease in physical functions may be addressed as early as possible, maintaining an acceptable QoL before and after radiotherapy [28,31]. In addition, the inclusion of pre-intervention protocols could enable operators to give patients the necessary information and reduce the concern due to the disease and treatment, thus limiting the deterioration of psychological aspects of QoL [18,32]. Further research will be needed in the future to assess the effectiveness of preventive dental procedures performed before radiotherapy, to improve post-treatment QoL and to increase survival of HNC patients.

Conclusions

Considering the limitations, this pilot study showed that fear of recurrence is the most important domain for HNC patients undergoing radiotherapy. The component of QoL that worsens most is the physical component, linked to oral functions such as saliva, taste and swallowing. As QoL is an important factor in patient survival, it will be important to act on the prevention of oral disease symptoms that can make QoL worse.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethical approval

This study was performed in line with the pronciples of the Declaration of Helsinki. The study received a favorable opinion from the Ethics Committee of A.O.U. Città della Salute e della Scienza of Turin (ref. 000030 of 07/01/2025).

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Financial interests

All authors declare they have no financial interests.

CRediT authorship contribution statement

Jacopo Lanzetti: Writing – original draft, Methodology, Data curation, Conceptualization. **Federica Ferrati:** Data curation. **Matteo Bartolomeo:** Investigation, Data curation. **Armando Crupi:** Supervision, Data curation. **Umberto Gibello:** Methodology, Data curation. **Federico Mussano:** Writing – review & editing. **Francesco Pera:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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