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ORIGINAL ARTICLE

The influence of xerostomia after radiotherapy on quality of life

Results of a questionnaire in head and neck cancer

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Abstract
Introduction Xerostomia is a common complication of radiotherapy for head and neck cancer because irreparable damage is caused to the salivary glands if they are included in the radiation fields. The aim of the study was to evaluate the degree of xerostomia in survivors of head and neck cancer and to determine its impact on quality of life.
Methods and materials A xerostomia questionnaire consisting of three parts (xerostomia score, quality of life survey, and visual analogue scale) was completed by 75 head and neck cancer patients, more than 6 months after radiotherapy and without evidence of disease.
Results The majority of patients (93%) suffered from a dry mouth, and 65% had moderate to severe xerostomia (grade 2 to 3). Both dysphagia (65%) and taste loss (63%) were common, although oral pain was less frequent (33%). The emotional impact of xerostomia was significant, causing worry (64%), tension (61%), or feelings of depression (44%). Furthermore, patients reported problems with talking to (60%) or eating with (54%) other people and to feel restricted in amount and type of food (65%). Quality of life was influenced by T classification, clinical stage, a higher radiation dose or the use of concomitant chemotherapy, but was independent of the interval since the end of radiotherapy.
Conclusions Xerostomia after radiotherapy for head and neck cancer is extremely common and significantly affects quality of life. No recuperation is seen over time, and the use of concomitant chemotherapy significantly increases the oral complications of radiation. These results warrant the continuing efforts put into the development of salivary gland-sparing radiotherapy techniques and effective treatments of radiation-induced xerostomia.

Keywords Head and neck · Radiotherapy · Xerostomia · Quality of life · Salivary glands

Introduction

There will be an estimated 39,250 new cases of head and neck cancer (HNC) in the USA in 2007, resulting in 11,090 deaths [18]. Radiotherapy (RT) is a common treatment for HNC, yet it produces considerable acute and long-term side-effects. One of the most frequent complications of conventional RT is xerostomia because the major salivary glands are usually included in the radiation portals [6]. Patients suffer from oral discomfort or pain, find it difficult to speak, chew, or swallow, and run an increased risk of dental caries or oral infection [13]. No effective treatment for xerostomia exists, so prevention is mandatory [23]. New radiation techniques allow partial sparing of the salivary glands, whereby permanent xerostomia can be avoided [5, 20].

There are various ways of recording salivary gland toxicity [9]. Measurements of salivary flow rate are currently the most commonly applied objective measures of salivary gland function [24]. Imaging techniques, such as salivary gland scintigraphy or magnetic resonance imaging, can also be used to evaluate hyposalivation [25, 26]. However, because xerostomia is defined as a symptom, it is equally important

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to estimate the subjective appreciation of oral dryness by the patient. Recent evidence suggests that patient self-reported scores, rather than physician-assessed scores, should be the main end points in evaluating xerostomia [21]. Despite the considerable psychological and social impact of xerostomia, few studies to date addressed the extent of its influence on quality of life (QoL). This is unfortunate because it is necessary to evaluate the effectiveness of new treatment strategies not only in terms of tumor control or survival but also to take into account acute or late morbidity and QoL.

The purpose of this study was to describe the incidence and severity of permanent xerostomia and its impact on QoL in a representative group of HNC patients who were at different intervals after RT and who received different treatment schedules, focusing solely on patient-reported symptom scoring.

Methods and materials

Patient population

Seventy-five patients, previously treated with RT for HNC at the Leuven department, were asked to complete a xerostomia questionnaire (XQ) while waiting for their regular follow-up visit at the multidisciplinary outpatient clinic of head and neck

Table 1 Xerostomia questionnaire (XQ)

Symptoms	Scale				
Part 1: Xerostomia grade					
Xerostomia					
No xerostomia	0				
Now and then, partial	1				
Always, partial	2				
Completely dry, disturbing	3				
Pain					
No pain	0				
Seldom, minimal	1				
Always, strong	2				
Unbearable	3				
Taste loss					
No change	0				
Seldom, minimal	1				
Now and then, considerable	2				
Always	3				
Dysphagia					
No swallowing problems	0				
Solid food	1				
Soft food	2				
Liquids	3				
Part 2: Quality of Life (QoL)					
My dry mouth…	Not at all (1)	A little (2)	Moderately (3)	Quite a lot (4)	Very much (5)
Restricts the amount and type of food I eat					
Gives me an uncomfortable feeling in my mouth					
Makes me worry					
Restricts my social life					
Makes it awkward to eat in front of other people					
Makes it difficult to speak to other people					
Is the cause of considerable tension					
Makes me worry about the look of my teeth and mouth					
Makes me feel depressed					
Restricts me in my daily activities					
Troubles my intimate relation					
Gives my food less or a different taste					
Diminishes my will to live					
Invades every aspect of my live					
Cannot stay like this for the rest of my life					
Part 3: Visual Analogue Scale (VAS)					

oncology. The coordinator explained the study to each participant, who read and signed an informed consent form; all 75 patients agreed to participate. The Ethics Committee of the University Hospital Leuven granted approval for the study.

Patients eligible to participate in the study were aged 18 years or older and had completed RT for HNC (total dose > 50 Gy), with the field of irradiation encompassing the major salivary glands bilaterally (mean gland dose > 35 Gy), at least 6 months earlier. Patients who had evidence of persisting or recurrent malignant disease were not included, as were patients with Sjögren's syndrome or other medical causes of xerostomia. None of the patients received any treatment for xerostomia (e.g., saliva substitutes or stimulants) other than frequent sips of water and had not received any measures to prevent xerostomia (e.g., salivary gland-sparing RT or concomitant amifostine).

Xerostomia questionnaire

The XQ consisted of three parts (Table 1) [7]. First, patients were asked to estimate the degree (grade 0 to 3) of xerostomia, oral pain, taste loss, and dysphagia they were suffering from and to state if they had increased tooth decay or problems with dentures since RT (yes or no). Second, participants answered 15 questions, regarding the perceived impact of xerostomia on their QoL. For each question, patients encircled a number from 1 to 5, reflecting the measure of agreement with the statement. A QoL score was calculated (100—sum of all scores) to provide an impression of the general impact of xerostomia on QoL. Third, the XQ also included a 100-mm Visual Analogue Scale (VAS) on which patients could mark to which degree they suffered from xerostomia, with one end representing no xerostomia (completely normal saliva) and the other end total xerostomia (no saliva at all). The VAS score can be arbitrarily translated into a four-grade xerostomia scale:

Grade 0 = VAS score of 24 or less
Grade 1 = VAS score between 25 and 49
Grade 2 = VAS score between 50 and 74
Grade 3 = VAS score of 75 or more

All patients completed the XQ in privacy and without help or interference.

Statistical analysis

Patient and tumor characteristics (age, gender, primary site, TNM classification, clinical stage, radiation dose, treatment modality, and interval since end of RT) were recorded. The data were analyzed using the software package Statistica 7® (StatSoft, Tulsa, OK). The significance and independence of each parameter (age, gender, T classification, N classification, clinical stage, surgery, concomitant chemotherapy, radiation dose, and time since end of RT treatment) in predicting the degree of xerostomia patients suffered from was tested using multiple linear regression. A correlation was examined between the xerostomia symptom score, QoL score, and VAS score. A p value of less than 0.05 was considered significant.

Results

Seventy-five patients were included in the statistical analysis; all had received RT treatment for HNC, with the field of irradiation encompassing the major salivary glands bilaterally. Patient and tumor characteristics are summarized in Table 2. There were 60 male (80%) and 15 female (20%) patients, with a mean age of 64 years (range, 45–89 years). Treatment was decided by a multidisciplinary team according to institutional guidelines: 34 patients (45%) underwent surgery followed by RT, 26 (35%) received definitive RT, and 15 (20%) were treated with concomitant

Table 2 Patient and tumor characteristics

Characteristics	Number of patients	Percent
Age		
≤60 years	33	44
>60 years	42	66
Gender		
Male	60	80
Female	15	20
Primary site		
Larynx	29	39
Oral cavity	18	24
Oropharynx	17	23
Hypopharynx	11	15
Surgery preradiotherapy		
Yes	34	45
No	41	55
Concomitant chemotherapy		
Yes	15	20
No	60	80
T classification		
T1	22	29
T2	11	15
T3	15	20
T4	27	36
N classification		
N0	36	48
N1	16	21
N2	23	31
Clinical stage		
Stage I	17	23
Stage II	5	7
Stage III	18	24
Stage IV	35	47

chemoradiotherapy. The mean total dose was 63.2 Gy (range, 50–72 Gy; median dose 66±8.6 Gy). In all patients, a conventional radiation technique was used with two opposing lateral beams and one lower neck field for the supraclavicular regions. The mean follow-up time since the end of RT was 35.7 months (range, 6–156 months).

Xerostomia questionnaire

A large majority of patients (*n*=70; 93%) complained of xerostomia (grade 1 to 3), and more than half of patients (*n*=40, 53%) suffered from severe xerostomia (grade 3). Only five patients (7%) did not report any dryness of the mouth. The second most frequent complaint was dysphagia (*n*=49, 65%), followed by taste loss (*n*=47, 63%). A minority of patients complained from pain (*n*=25, 33%). These results are shown in Fig. 1. Increased difficulties with dentures was reported by 59% (*n*=10) of patients who had dentures before treatment (*n*=17). Of subjects who were dentate before RT (*n*=58), 64% (*n*=37) reported augmented tooth decay, and 28% (*n*=16) needed dentures after RT.

Xerostomia had an important impact on QoL (Table 3). The mean QoL score was 65.6 (range, 32–85; the median QoL score was 67±13.1). Responses regarding emotional

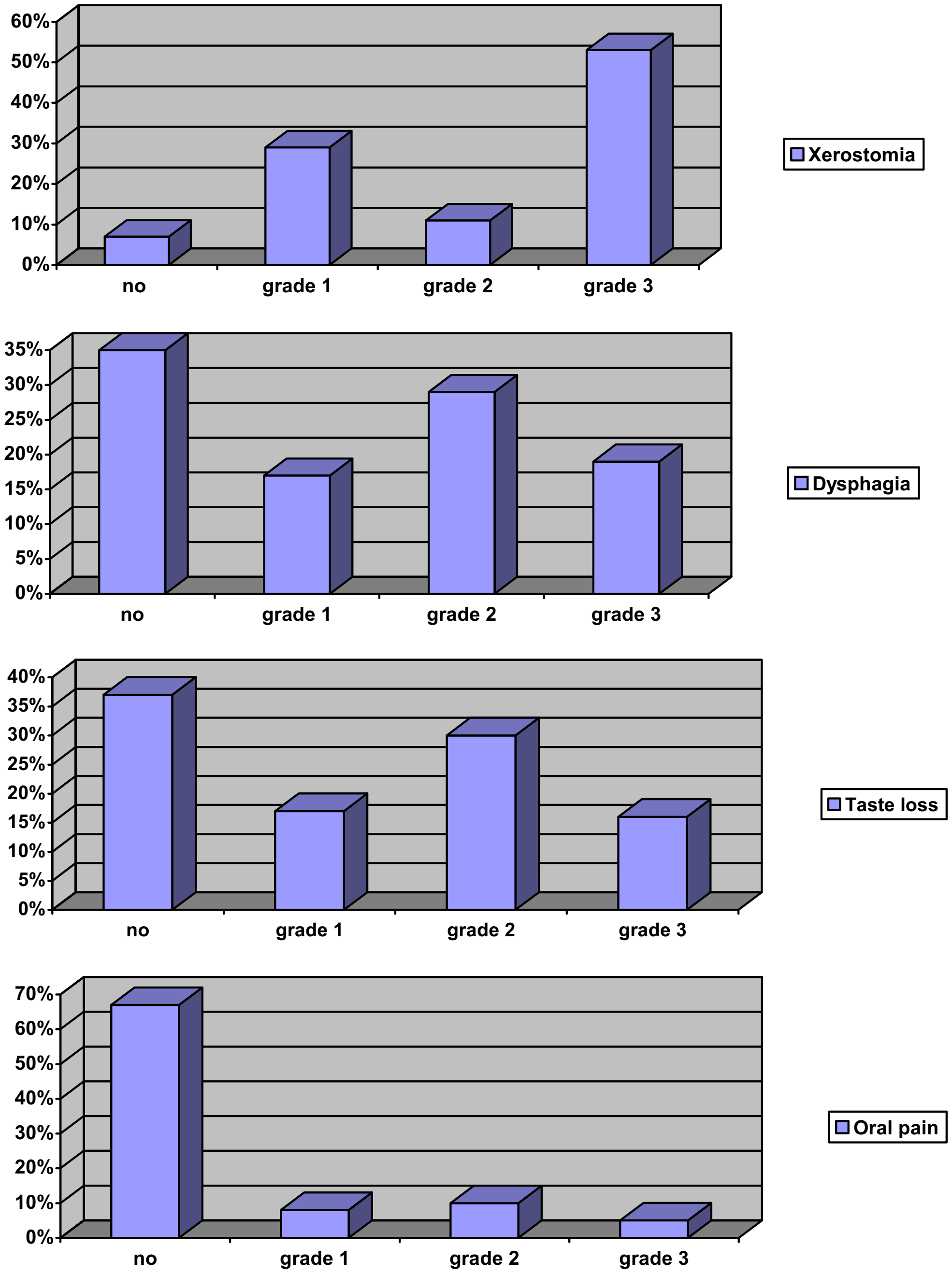

Fig. 1 The overall majority of patients (*n*=70; 93%) complained of moderate to severe xerostomia (grade 1–3), and more than half of patients (*n*=40, 53%) suffered from severe xerostomia (grade 3). Only five patients (7%) did not report any dryness of the mouth. The second most frequent complaint was dysphagia (*n*=49, 65%), followed by taste loss (*n*=47, 63%). Only a minority of patients complained from pain (*n*=25, 33%)

Table 3 Results of the QoL part of the xerostomia questionnaire (XQ)

My dry mouth…	Not at all (1)	A little (2)	Moderately (3)	Quite a lot (4)	Very much (5)
Restricts the amount and type of food I eat	26 (35%)	6 (8%)	9 (12%)	16 (21%)	18 (24%)
Gives me an uncomfortable feeling in my mouth	15 (20%)	6 (8%)	19 (25%)	17 (23%)	18 (24%)
Makes me worry	27 (36%)	19 (25%)	13 (17%)	12 (16%)	4 (6%)
Restricts my social life	42 (56%)	11 (15%)	10 (13%)	9 (12%)	3 (4%)
Makes it awkward to eat in front of other people	35 (46%)	11 (15%)	6 (8%)	12 (16%)	11 (15%)
Makes it difficult to speak to other people	30 (40%)	15 (20%)	10 (13%)	18 (24%)	2 (3%)
Is the cause of considerable tension	29 (39%)	16 (21%)	10 (13%)	11 (15%)	9 (12%)
Makes me worry about the look of my teeth and mouth	41 (55%)	7 (9%)	12 (16%)	10 (13%)	5 (7%)
Makes me feel depressed	42 (56%)	13 (17%)	13 (17%)	3 (4%)	4 (6%)
Restricts me in my daily activities	49 (65%)	12 (16%)	5 (7%)	6 (8%)	3 (4%)
Troubles my intimate relation	60 (80%)	1 (1%)	8 (11%)	5 (7%)	1 (1%)
Gives my food less or a different taste	27 (36%)	8 (11%)	10 (13%)	15 (20%)	15 (20%)
Diminishes my will to live	46 (61%)	16 (21%)	6 (8%)	3 (4%)	4 (6%)
Invades every aspect of my live	41 (55%)	16 (21%)	9 (12%)	4 (6%)	5 (7%)
Cannot stay like this for the rest of my life	15 (20%)	4 (6%)	12 (16%)	13 (17%)	31 (41%)

functioning showed more than half of the patients reporting worry (64%) or tension (61%), to the point where 45% of patients thought that their dry mouth invades every aspect of their life, and 44% of patients felt "depressed." Complaints were reported as "quite a lot" or "very much" for tension by 27%, worry by 22%, and depression by 10% of patients. No less that 39% stated that their dry mouth diminishes their will to live, with 6% answering "very much" on that particular question. Responses to questions on social functioning showed comparable results. Approximately half of patients reported problems with talking to (60%) or eating with (54%) other people and were therefore constrained in their social life (44%) or daily activities (35%). In a similar vein, 45% of patients worried about the look of their teeth and mouth. A minority of patients reported problems in their intimate relationships (20%).

The QoL questionnaire also included a part on oral symptoms, showing analogous results as the xerostomia score. Oral discomfort was reported by the majority of patients (80%) and was reported as "quite a lot" to "very much" by 47% of patients. Xerostomia has a substantial impact on the way patients eat because 65% of patients felt restricted in amount and/or type of food, one fourth (24%) even "very much" so. In 64% of patients, the food they ate has less or changed taste. Ultimately, an overwhelming majority of patients, 80%, felt that it would be a dire prospect to live with the level of xerostomia they had at that time point, at least 6 months after the end of treatment, for the rest of their lives.

Regarding the VAS score, the mean score was 52.8 (range, 0–100; the median score was 54 ± 35.5). When translated into a xerostomia grade, 21 patients (28%) scored grade 0, 11 (14%) grade 1, 17 patients (23%) grade 2, and 26 patients (35%) reported grade 3 xerostomia.

Statistical analysis

The reported grade of xerostomia was significantly and independently predicted by more advanced clinical stage (relative risk [RR] 2.03, 95% confidence interval [CI] 2.57–

Table 4 Results of multivariate analysis

Variable	Xerostomia	Dysphagia	Pain	VAS	QoL
Gender (M vs F)	–	–	–	–	–
Age (< vs ≥55 years)	–	–	–	–	–
T classification (T1–2 vs T3–4)	0.06	–	–	–	0.04
N classification (N0 vs N+)	–	–	–	–	–
Clinical stage (SI–II vs SIII–IV)	0.02	0.06	–	–	0.02
CT (no vs yes)	0.005	0.002	0.01	–	0.04
Surgery (no vs yes)	–	–	0.04	–	–
Dose (< vs ≥60 Gy)	0.006	0.04	–	0.02	0.01
Time since RT (< vs ≥2 years)	–	–	–	–	–

Taste loss was not significantly associated with any of the variables in multivariate analysis and is consequently not shown

CT Concomitant chemotherapy, *RT* radiotherapy, *M* male, *F* female

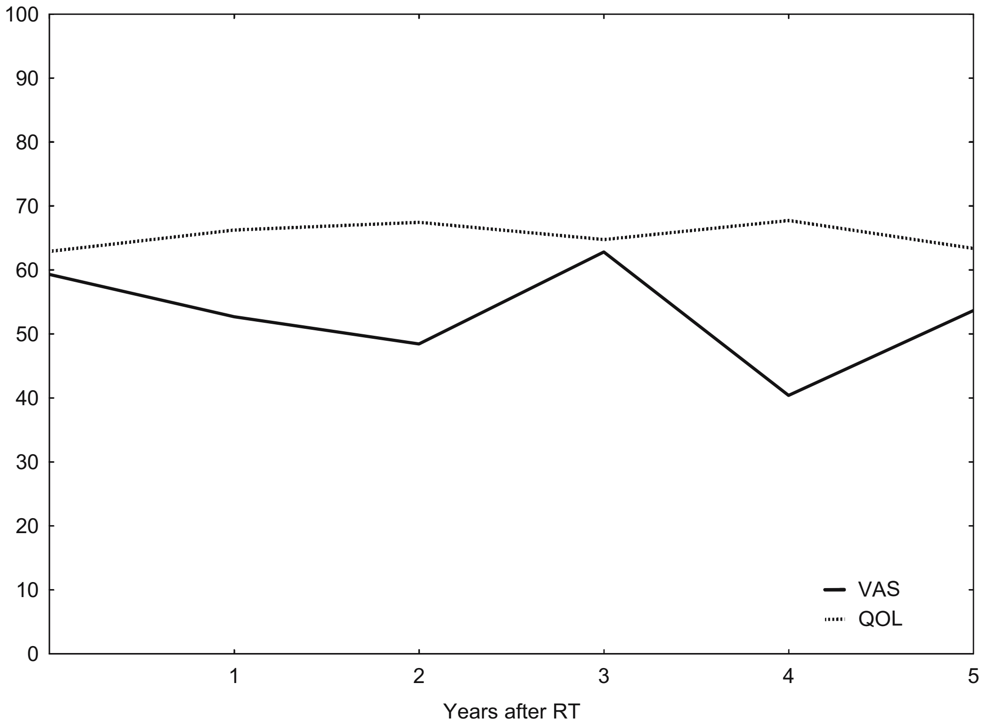

Fig. 2 Mean VAS and QoL scores over time. High scores imply a high level of symptoms for VAS; a higher QoL score implies a better quality of life

1.48, $p=0.02$), the use of chemotherapy (RR 1.42 [95% CI 1.65–1.18], $p=0.005$), and a radiation dose larger than or equal to 60 Gy (RR 1.58 [95% CI 1.58–1.15], $p=0.006$). There was a trend toward statistical significance with the T classification ($p=0.06$). Results are shown in Table 4. The incidence of dysphagia was significantly associated with use of chemotherapy (RR 1.45 [95% CI 1.68–1.23], $p=$ 0.002) and a dose greater than or equal to 60 Gy (RR 1.26 [95% CI 1.48–1.04], $p=0.04$). A trend toward statistical significance was observed between clinical stage and reported swallowing problems ($p=0.06$). Both the use of chemotherapy (RR 1.37 [95% CI 1.61–1.13], $p=0.01$) and surgery (RR 1.29 [95% CI 1.53–1.05], $p=0.04$) significantly and independently predicted patient-reported oral

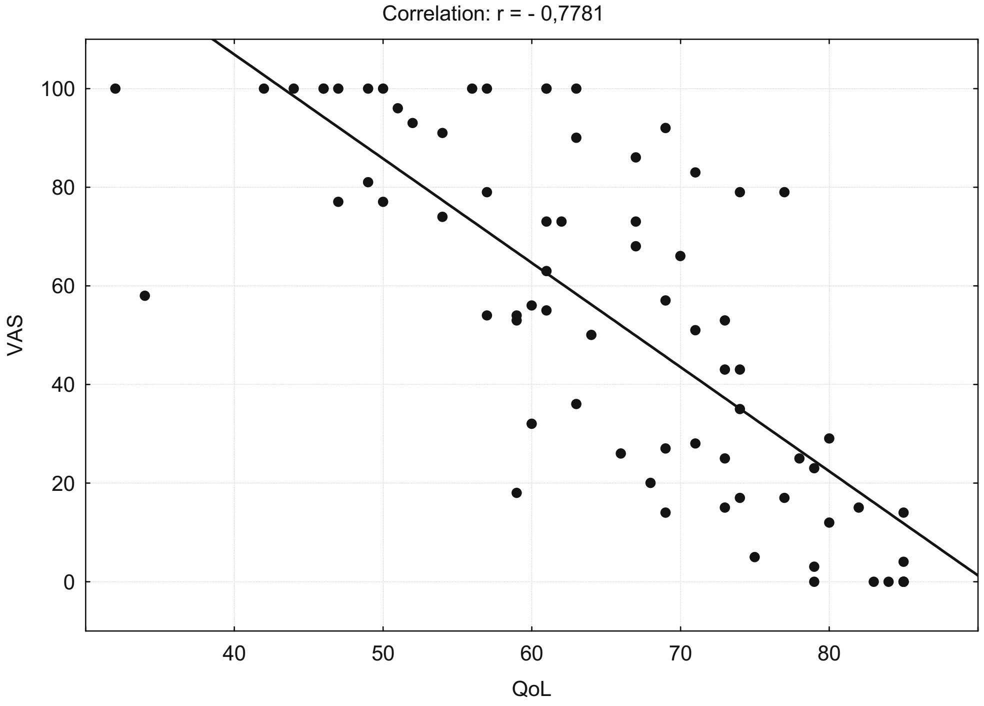

Fig. 3 Linear correlation between VAS score and QoL score

pain. Taste loss could not be predicted by any of the variables in multivariate analysis. A higher VAS score was significantly associated with a dose greater than or equal to 60 Gy (RR 1.32 [95% CI 1.55–1.10], $p = 0.02$).

Impact on QoL could be significantly and independently predicted by more advanced T classification (RR 1.57 [95% CI 1.99–1.14], $p = 0.04$) and clinical stage (RR 1.94 [95% CI 2.50–1.39], $p = 0.02$), the use of chemotherapy (RR 1.28 [95% CI 1.53–1.04], $p = 0.04$), and a dose greater than or equal to 60 Gy (RR 1.34 [95% CI 1.56–1.12], $p = 0.01$). Within the QoL questionnaire, chemotherapy was associated with increased restriction of the amount and type of food ($p = 0.003$), uncomfortable feeling in the mouth ($p = 0.009$), and difficulty with eating in front of other people ($p = 0.005$), all reflecting oral dysfunction. Radiation dose was predominantly associated with the patient's well-being, a dose greater than or equal to 60 Gy significantly and independently predicted feelings of tension ($p = 0.0005$) and depression ($p = 0.04$), social inadequacy ($p = 0.04$), worry about the look of teeth and mouth ($p = 0.0005$), and perceived difficulty in intimate relationships ($p = 0.03$).

For the xerostomia score, VAS score, and QoL, no significant correlation was seen with the time since RT (Table 4), and there was no improvement seen in the VAS score as well as QoL score with time (Fig. 2).

A significant correlation was found between VAS and QoL scores ($r = -0.78$, Fig. 3), xerostomia grade and VAS score ($r = 0.67$), and between xerostomia grade and QoL score ($r = -0.67$).

Discussion

Xerostomia is a serious and almost ubiquitous complication after RT for head and neck malignancies [6]. At minimally 6 months since the end of treatment, 93% of all patients complained of a dry mouth and 65% experienced moderate to severe (grade 2 or 3) xerostomia. These percentages are consistent with two earlier studies regarding the incidence of xerostomia in HNC patients. Epstein et al. [11] found that 77.8% of 65 patients, surveyed more than 6 months after conventional RT, suffered from moderate to severe xerostomia; only 9.2% did not report any dryness of the mouth. Wijers et al. [29] from the University of Rotterdam determined that 64% of 39 long-term survivors (at least 2 years follow-up) suffered from moderate to severe xerostomia; all surveyed patients complained to some degree of a dry mouth. This high percentage of long-lasting xerostomia in HNC survivors warrants the continuing efforts put into the improvement of salivary gland-sparing RT techniques and the development of effective treatments [5, 20]. The impact of xerostomia on oral health is quite substantial, and this study provides further evidence of the xerostomia syndrome [6]. Most surveyed patients complained of dysphagia, taste loss, and difficulty with dentures or increased tooth decay.

One of the purposes of this study was to measure the impact of xerostomia on QoL. The emotional strain of living with xerostomia seems quite significant: A large proportion of patients felt worried (64%), tense (61%), or even depressed (44%) because of their dry mouth. Furthermore, patients were severely limited in their social activities: The majority did not like to talk to (60%) or eat with (54%) other people. These results are all the more telling because it was the impact of xerostomia alone that was measured. Earlier studies already reported seriously diminished QoL in survivors of HNC, and xerostomia seems to play a substantial role in this [1, 2, 8, 12, 14, 15, 19, 22, 27, 28]. This is further demonstrated by the correlation between xerostomia grade as well as VAS score and QoL in our report.

The use of concomitant chemoradiotherapy in the treatment of HNC could possibly increase the incidence and severity of acute and late complications [16]. In this analysis, the use of concomitant chemotherapy was associated with a significantly increased risk of xerostomia, dysphagia, mouth pain, and with decreased QoL. Traditionally, management of cancer has focused on clinical outcome, e.g., loco-regional control and survival. QoL is an additional series of outcome measures that may have important ramifications in the decision-making process, particularly when different treatment options are expected to result in similar tumor response. QoL must be assessed in future trials of patients with HNC to determine treatment that results in the best chance of cure with the least impact on oral function.

It was recently suggested that there might be significant recovery of salivary gland function, even many years after RT. Braam et al. [3, 4] found an increase in salivary flow rate of approximately 32% from 12 months to 5 years after RT. This notion is not confirmed by the results of this study. Although there was significant variation in the time that had elapsed since the end of treatment (a range of 6 months to 13 years), neither xerostomia nor its impact on swallowing, taste loss, pain, or QoL was influenced by the interval since RT (Fig. 2). This seems to validate earlier assumptions that there is very little recovery over time in patients who did not receive some sort of parotid-sparing technique [10]. Indeed, even habituation, the subjective impression that the severity of any chronic disease decreases with time, seems absent when it comes to xerostomia.

Several limitations to our study should be noted. First, this was a cross-sectional study whereby we included all patients meeting the inclusion criteria during several follow-up consultations until accrual was completed (required number was 75). Obviously, this methodology cannot exclude the possibility of some selection bias, although all solicited patients agreed to participate and completed the questionnaire. Second, we did not compare results with an age- and/or sex-matched control group of noncancer or non-HNC cancer patients. It is clear that xerostomia and other oral complaints are not uncommon in the healthy (elderly) population and even more so in cancer patients [6, 23]. However, the very high incidences seen in this report are inevitably linked to RT. Third, we did not correlate the subjective, patient-reported symptom scoring with objective measurements of salivary function, such as parotid flow measurements, which would have further elucidated the relationship between lack of saliva production and subjective xerostomia. Although, it should be noted that often only a limited correlation between salivary flow and xerostomia symptoms is found [21]. Fourth, the XQ that was used in this study was deliberately kept very straightforward, so that all patients could complete it without a researcher present [17]. This questionnaire was already used and validated in a study evaluating the efficacy of a saliva substitute [7]. The QoL part consists of xerostomia-related questions selected from several different validated HNC-specific QoL questionnaires [1, 4, 6, 8, 11, 15, 27, 28]. However, it is certainly advisable to employ one well-validated and widely used questionnaire in future trials, if only to facilitate comparison between studies.

Conclusion

Xerostomia after RT for HNC is extremely common and significantly affects QoL. No recuperation is seen over time, and the use of concomitant chemotherapy could increase the oral complications of radiation. These results warrant the continuing efforts put into the further improvement of salivary gland-sparing radiation techniques and the development of effective treatment for radiation-induced xerostomia.

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Conflict of interest All authors have read and approved the manuscript; we have no conflicts of interest to declare or financial support from industry sources to disclose.

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