Supportive Care in Cancer (2020) 28:1941–1950
https://doi.org/10.1007/s00520-019-05008-4

ORIGINAL ARTICLE

Clinical and sociodemographic factors that affect the quality of life of survivors of head and neck cancer

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Received: 17 January 2019 / Accepted: 24 July 2019 / Published online: 2 August 2019

Abstract

Objective The present cross-sectional study evaluated the quality of life of patients treated with 3-D conformal radiotherapy for cancer of the mouth, oropharynx, hypopharynx, or larynx and investigated possible associations with clinical and sociodemographic variables using multivariate analysis.

Methods The sample was composed of 90 patients who had completed treatment at least 3 months earlier. Data were collected from April 2016 to May 2017. The patients were clinically evaluated with regard to stimulated salivary flow, trismus, and radiation caries. Sociodemographic data and data related to the disease (stage, location of primary tumor, and radiation dose) were collected from the patient charts. Quality of life was assessed using the Brazilian version of the University of Washington Quality of Life (UW-QOL) questionnaire. Poisson logistic regression was performed to determine the mean ratio and test associations with the clinical and sociodemographic variables.

Results The mean total of the UW-QOL was 814.88 (± 224.58). Patient age, staging of cancer, hyposalivation, and trismus were associated with quality of life. Patients with tumors in the advanced stage, those with hyposalivation and those with trismus respectively had 11% (CI 0.80–0.98), 12% (CI 0.79–0.99), and 15% (CI 0.77–0.94) lower UW-QOL scores, indicating poorer quality of life.

Conclusion Survivors of head and neck cancer experience a negative impact on quality of life associated with trismus, hyposalivation, advanced stage tumors, and a younger patient age. The present findings underscore the importance of a specific approach focused on these aspects to ensure better quality of life in the long term.

Keywords Quality of life · Radiotherapy · Head and neck cancer · Trismus · Hyposalivation

Introduction

Radiotherapy (RT) is an important therapeutic modality for the treatment of patients with head and neck cancer as primary treatment, an adjuvant to surgery, employed concomitantly to chemotherapy or as palliative therapy [1]. However, high doses of RT can result in both acute and late-onset adverse effects. Moreover, RT can exert a negative impact on quality of life, affecting physical, social, and emotional factors during and after treatment [2].

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Over the years, quality of life has been the object of numerous studies and is considered an important outcome that results from the interaction between general health conditions and both social and contextual factors [3, 4]. The University of Washington Quality of Life (UW-QOL) questionnaire is one of the main tools for the assessment of health-related quality of life of patients with head and neck cancer [5].

Recent studies have demonstrated that patients in RT for the treatment of head and neck cancer experience a greater negative impact on quality of life compared to patients who are free of the disease [6]. Other studies have compared quality of life of patients before and during RT and also found that quality of life is impacted more negatively during treatment [7].

A large number of investigation studies in the literature on the quality of life of patients with head and neck cancer have prioritized the analysis of sociodemographic characteristics and have administered the questionnaire at the time of diagnosis or during treatment. Thus, there is a lack of studies that have evaluated patients after the completion of treatment analyzing the impact of the late-onset effects of RT on the quality of life of survivors of head and neck cancer through the investigation of clinical variables. The consensus in the literature is that RT has a number of late-onset effects, such as trismus (limited mouth opening), hyposalivation (reduced salivary flow), and radiation caries [8]. These manifestations of the toxicity of treatment are each known to affect quality of life [8]. However, no previous study has performed multivariate analysis to determine which of these factors exerts a greater impact on quality of life.

Considering the importance of individualized oncological treatment, which can maximize quality of life in the long term [9], the aim of the present study was to evaluate the association between the late-onset adverse effects of RT and quality of life among survivors of cancer of the mouth, oropharynx, hypopharynx, or larynx using objective measures of clinical variables and multivariate analysis.

Materials and methods

Study design and participants

An observational, quantitative, analytical, cross-sectional study was conducted with survivors of cancer of the mouth, oropharynx, hypopharynx, or larynx treated with 3-D conformal RT at the Santa Maria University Hospital, which is a reference hospital in the state of Rio Grande do Sul, Brazil, for 42 municipalities and more than one million inhabitants. The patients were invited to participate in the study when returning to the head and neck outpatient clinic for follow-up. After receiving clarifications regarding the purpose and procedures of the study, those who agreed to participate signed a statement of informed consent. This study received approval from the Human Research Ethics Committee of University Federal of Santa Maria (protocol number 51958915.6.0000.5346; certificate number 1.387.994).

The inclusion criteria were male or female patients aged 18 years or older who had been treated with 3-D conformal RT for cancer of the mouth, oropharynx, hypopharynx, or larynx and who had completed treatment at least 3 months earlier. By convention, late-onset adverse events appear 3 or more months after the completion of radiotherapy [10]. The exclusion criteria were a recurrence of the disease or new primary tumor and an inability to participate in the proposed evaluations and clinical examinations. Data were collected from April 2016 to May 2017. Considering an 85% confidence interval (CI) and 5% margin of error, the minimum sample size was determined to be 86 individuals. The sample size ($n = 144$) was calculated considering six new eligible patients per week over a 6-month period (time scheduled for the follow-up evaluation after the completion of treatment).

Data collection

Quality of life was assessed using the UW-QOL questionnaire for patients with head and neck cancer, which has been translated into Portuguese and validated for use on the Brazilian population [11]. The medical history (location of tumor, staging, type of treatment, total radiation dose, comorbidities/drugs that could cause xerostomia, and time elapsed since the completion of treatment) was obtained from the patient charts. The sociodemographic data were reported by the participants themselves.

The UW-QOL (4th edition) is questionnaire developed for to measure the quality of life of patients with head and neck cancer and is one of the most widely used quality of life assessment tools in the world [12]. The questionnaire is composed of 12 multiple-choice items distributed among the following subscales: pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, and anxiety. Besides the objective items, the respondent is also asked to mark which three subscales were the most important in the previous 7 days. The UW-QOL ends with three questions by which the respondent classifies quality of life considering the family, social, and spiritual contexts and offers the opportunity for the respondent to describe any other issues important to his/her quality of life that were not addressed on the questionnaire. Each item has a three to five response options with scores ranging from 0 to 100. Lower scores denote a greater negative impact on quality of life. Each of the 12 subscales can be evaluated either separately or together using either the mean or total [5, 7].

After completing the questionnaire, the clinical examination was performed to evaluate the dentition, the occurrence of radiation caries, trismus, xerostomia, and hyposalivation. Radiation caries was recorded when ring-shaped carious

lesions were found on the vestibular and lingual faces of the cervical third of the teeth [13]. The examination was performed in a dental chair with a reflector in a well-lit room. Two examiners had previously been trained and calibrated for this evaluation by analyzing 20 images on a computer. The analysis of the images was repeated after approximately 30 days. Intra-examiner and inter-examiner agreements were determined using the Kappa coefficient, which ranged from $\kappa = 0.79$ to 1.00.

Mouth opening was measured using a millimeter ruler, and trismus was recorded when mouth opening was equal to or less than 35 mm [14]. Xerostomia was evaluated based on the response to the following question: "Does your mouth generally feel dry?" [15]. An affirmative answer was considered a positive indication of xerostomia (subjective sensation of dry mouth). Hyposalivation was determined based on stimulated salivary flow following the methods proposed by Navazesh and Kumar [16] and Thomson [17] and was recorded when stimulated salivary flow was equal to or less than 0.5 mL/min (Sreebny) [18].

Data analysis

The data were analyzed descriptively, with the calculation of mean, standard deviation, median, and percentage values. Either the Kolmogorov-Smirnov or Shapiro-Wilk test was used to determine the homogeneity of the samples. The overall mean and standard deviation of the UW-QOL was calculated. For statistical purposes, age, radiation dose, and time elapsed since the completion of treatment were dichotomized by the median; location of the primary tumor was dichotomized as mouth and oropharynx or hypopharynx and larynx; staging was dichotomized as early (stages I and II) or advanced (stages III and IV); and type of treatment was dichotomized as 3D conformal RT with or without concomitant chemotherapy. The Mann-Whitney test was used to compare the mean UW-QOL subscale scores to the clinical and demographic variables. The mean ratio was calculated through Poisson regression analysis with robust variance. The variables incorporated into the crude model were age, tumor location, staging, type of treatment, radiation dose, time elapsed since the completion of treatment, hyposalivation, trismus, and comorbidities/drugs that could cause xerostomia. Only variables with a p value < 0.05 in the crude model were incorporated into the adjusted model. The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 21.0, PASW, Chicago, IL, USA).

Results

Among the 98 patients invited to participate in the study, 90 underwent the clinical examinations and answered the questionnaire (response rate 91.8%). Non-participation was due to the impossibility of staying for the evaluation because of the public transportation schedule. Most participants had self-declared white skin color (87.8%), were male (87.8%), and had an incomplete primary school education (76.7%). The mean radiation dose during 3D conformal RT was 62.99 Gy (± 9.74) and mean time elapsed since the completion of treatment was 35.59 months (± 37.60). Mean age was 62.33 (± 9.70) and patients younger than 62 years of age had lower UW-QOL scores. Most tumors were diagnosed in an advanced stage (III and IV) and were located in the mouth and oropharynx (60.0%). Mean mouth opening was 32.91 mm (61.10 ± 19.89). Trismus was found in 48.9% of the sample and those with this condition had a worse mean UW-QOL score. The majority (75.6%) exhibited hyposalivation, and mean stimulated salivary flow was 0.47 mL/min (64.64 ± 18.17) Table 1.

Among the 12 subscales on the UW-QOL questionnaire, the lowest means were found on the saliva (51.79) and taste (57.38) subscales, indicating worse quality of life (Table 2). Among the subscales considered, the most important to the patients in the previous 7 days, the most cited were saliva (56.7%), pain (31.1%), speech (26.7%), swallowing (23.3%), and taste (22.2%).

In the comparative analysis of the mean UW-QOL subscale scores according to the clinical and demographic variables, associations were found between age and the following subscales: pain ($p = 0.004$), appearance ($p = 0.015$), swallowing ($p = 0.004$), chewing ($p = 0.042$), shoulder ($p < 0.001$), and saliva ($p = 0.017$); patients aged less than 62 years had poorer scores on all these subscales, indicating worse quality of life. Individuals with tumors located in the mouth and oropharynx had lower scores on the pain ($p = 0.013$), swallowing ($p = 0.004$), chewing ($p < 0.001$), and saliva ($p = 0.006$) compared to those with tumors in the hypopharynx and larynx. Patients with advanced stage tumors had significantly lower scores on the pain, activity, chewing, and saliva subscales compared to those with early stage tumors. A shorter time elapsed since the completion of treatment was associated with lower scores on swallowing ($p = 0.026$), speech ($p = 0.004$), shoulder ($p = 0.004$), and saliva ($p = 0.039$) subscales, indicating worse quality of life. Patients with trismus had lower means scores on the recreation ($p = 0.027$), chewing ($p = 0.003$), saliva ($p = 0.021$), and anxiety ($p = 0.009$) subscales. Hyposalivation was associated with lower scores on appearance ($p = 0.006$), swallowing ($p = 0.005$), chewing ($p = 0.006$), taste ($p = 0.002$), and saliva ($p = 0.003$) subscales. Patients with comorbidities or drugs associated with xerostomia had lower scores on the activity ($p = 0.001$), recreation ($p = 0.004$), shoulder ($p = 0.005$), and anxiety ($p = 0.033$) subscales (Table 3).

Table 4 displays the multivariate analysis run to determine the mean ratio based on the total UW-QOL scores in relation to the independent variables: age, tumor location, staging,

Table 1 Mean UW-QOL score according to sociodemographic and clinical characteristics

Sociodemographic and clinical variables	*N* (%)	Mean UW-QOL ± SD
Sex		
Men	75 (83.3)	68.20 ± 18.61
Women	15 (16.7)	66.43 ± 19.84
Skin color		
White	79 (87.8)	68.11 ± 19.13
Non-White	11 (12.2)	66.41 ± 16.13
Age		
< 62 years	41 (45.6)	60.31 ± 19.86
≥ 62 years	49 (54.4)	74.26 ± 15.18
Schooling		
No formal study	2 (2.2)	61.83 ± 25.69
Incomplete primary school	69 (76.7)	69.27 ± 19.20
Complete primary school	10 (11.1)	64.55 ± 18.08
Incomplete high school	2 (2.2)	53.79 ± 29.17
Complete high school	7 (7.8)	64.98 ± 12.10
Tumor location		
Mouth and oropharynx	54 (60.0)	63.27 ± 19.31
Hypopharynx	5 (5.6)	78.88 ± 3.75
Larynx	31 (34.4)	74.22 ± 16.68
Stage*		
I	14 (15.6)	78.32 ± 16.75
II	13 (14.4)	72.98 ± 17.19
III	25 (27.8)	71.77 ± 18.64
IV	37 (41.1)	59.31 ± 17.14
Type of treatment		
Radiotherapy	6 (6.7)	66.79 ± 28.95
Surgery + radiotherapy	17 (18.9)	75.05 ± 17.50
Surgery + radiotherapy + chemotherapy	36 (40.0)	65.39 ± 17.69
Radiotherapy + chemotherapy	31 (34.4)	67.12 ± 18.26
Total radiation dose*		
≤ 66 Gy	42 (46.7)	64.31 ± 21.72
> 66 Gy	36 (40)	71.38 ± 15.76
Time since completion of treatment		
≤ 22 months	45 (50)	62.61 ± 17.22
> 22 months	45 (50)	73.20 ± 18.83
Xerostomia		
No	6 (6.7)	74.90 ± 19.61
Yes	84 (93.3)	67.41 ± 18.67
Dentition		
Normal	7 (7.8)	57.73 ± 19.45
Partially edentulous	61 (67.8)	68.84 ± 18.18
Edentulous	22 (22.4)	68.57 ± 19.87
Radiation caries		
No	46 (51.1)	67.22 ± 18.33
Yes	22 (24.4)	68.67 ± 19.18
Not applicable	22 (24.4)	
Trismus*		
No	42 (46.7)	74.61 ± 13.83
Yes	44 (48.9)	61.10 ± 19.89

Table 1 (continued)

Sociodemographic and clinical variables	*N* (%)	Mean UW-QOL ± SD
Hyposalivation		
No	20 (22.2)	79.77 ± 14.91
Yes	68 (75.6)	64.64 ± 18.17
Comorbidities/drugs that cause xerostomia		
No	42 (46.7)	72.85 ± 16.54
Yes	48 (53.3)	63.58 ± 19.58

*Missing data; *SD*, standard deviation

type of treatment, radiation dose, time elapsed since the completion of treatment, hyposalivation, trismus, and comorbidities/drugs that could cause xerostomia. In the crude model, age less than 62 years, tumor located in the mouth or oropharynx, advanced stage tumor, less than 22 months since the completion of treatment, hyposalivation, and trismus were associated with lower mean UW-QOL scores, indicating poorer quality of life. In the adjusted model, patients with advanced stage tumors ($p = 0.016$), hyposalivation ($p = 0.029$), and trismus ($p = 0.002$) had respectively 11% (CI 0.80–0.98), 12% (CI 0.79–0.99), and 15% (CI 0.77–0.94) lower mean UW-QOL scores, indicating poorer quality of life. Patients aged 62 ($p = 0.014$) or older had 1.17-fold (CI 1.03–1.33) higher mean UW-QOL scores, indicating a better quality of life.

Discussion

The present study evaluated the association between the late-onset adverse effects of 3-D conformal RT and sociodemographic factors on the quality of life of survivors of cancer of the mouth, oropharynx, hypopharynx, or larynx. The main findings were that age equal to or younger than 62 years, advance stage tumors, the presence of hyposalivation, and trismus were strongly associated with a poorer quality of life. To the best of our knowledge, this is the first study to associate clinical aspects of head and neck cancer with quality of life using the UW-QOL questionnaire and multivariate analysis.

Table 2 University of Washington Quality of Life (UW-QOL) questionnaire scores by subscale

UW-QOL (Subscales)	Mean ± SD	Median (P25–P75)
Pain	72.90 ± 29.85	75.00 (50.00–100.00)
Appearance	75.56 ± 20.86	75.00 (75.00–100.00)
Activity	71.33 ± 27.17	75.00 (50.00–100.00)
Recreation	73.33 ± 29.22	75.00 (50.00–100.00)
Swallowing	66.84 ± 30.87	67.00 (58.50–100.00)
Chewing	63.33 ± 35.00	50.00 (50.00–100.00)
Speech	67.46 ± 32.44	67.00 (33.00–100.00)
Shoulder	71.84 ± 33.93	100.00 (33.00–100.00)
Taste	57.38 ± 38.46	67.00 (33.00–100.00)
Saliva	51.79 ± 31.77	33.00 (33.00–67.00)
Mood	74.17 ± 31.46	100.00 (50.00–100.00)
Anxiety	68.94 ± 36.68	67.00 (33.00–100.00)
Total (sum)	814.88 ± 224.58	875.50 (625.00–991.25)

Herce-Lopez et al. [6] evaluated 60 patients following oncological treatment and found that individuals younger than 65 years of age had a poorer quality of life. This is in agreement with the present results, as the adjusted multivariate model was associated with negative impact on patients younger than 62 years of age. Such findings suggest that younger patients may experience greater stress and despondency and may be at greater risk of depression, as demonstrated by other authors [19]. In the comparative analysis of the UW-QOL and the independent variables, age was associated with pain, appearance, swallowing, chewing, shoulder, and saliva subscales. Although it seems surprising that patients older than 62 years of age have fewer salivary and chewing problems, Laraway et al. [20] suggest that older individuals may be better adapted after treatment and may be less concerned about body image, which may explain the differences in scores on the appearance subscale. The authors also suggest that older patients may be part of a smaller social group and interact with family members who are aware of post-treatment difficulties, thereby avoiding episodes of stress and facilitating both communication and eating [20].

Patients with advanced stage tumors had lower means on the UW-QOL and poorer quality of life in both models of the multivariate analysis, which is in agreement with findings described in previous studies [21]. This greater negative result may be explained by the more aggressive procedures used in advanced stages of the disease [22]. There is a consensus in the literature that advanced stage tumors require higher doses of radiation, which could lead to greater tissue damage and greater impairment of the salivary glands [8]. This would explain the significant associations found between tumor staging and the saliva, chewing, pain, and activity subscales, as higher doses of radiation reduce salivary production [10] and increase muscle fibrosis [23], causing pain and discomfort during chewing as well as contributing to a greater risk of developing trismus [21].

Table 3 Mean UW-QOL subscale scores according to demographic and clinical variables

Variables	UW-QOL subscales mean ± standard deviation											
Age	Pain	Appearance	Activity	Recreation	Swallowing	Chewing	Speech	Shoulder	Taste	Saliva	Mood	Anxiety
<62 years	63.68 ± 29.09	69.51 ± 22.72	64.63 ± 30.61	65.85 ± 32.96	56.17 ± 33.79	54.88 ± 36.75	65.88 ± 32.14	56.85 ± 36.79	49.51 ± 36.69	43.00 ± 30.16	69.51 ± 32.84	64.27 ± 39.05
≥62 years	80.61 ± 28.53	80.61 ± 17.87	76.94 ± 22.75	79.59 ± 24.30	75.78 ± 25.24	70.41 ± 32.14	68.78 ± 32.97	84.39 ± 25.57	63.96 ± 39.04	59.14 ± 31.51	78.06 ± 30.03	72.86 ± 34.49
p	*0.004*	*0.015*	0.067	0.050	*0.004*	*0.042*	0.605	*< 0.001*	0.075	*0.017*	0.156	0.323
Location												
Mouth and oropharynx	66.87 ± 29.91	72.22 ± 21.54	66.67 ± 29.14	68.98 ± 32.19	58.89 ± 32.48	50.00 ± 33.65	68.56 ± 30.74	68.50 ± 35.20	53.06 ± 38.66	44.33 ± 29.08	71.30 ± 33.44	69.81 ± 35.06
Hypopharynx and larynx	81.94 ± 27.78	80.56 ± 19.00	78.33 ± 22.52	79.86 ± 23.01	78.78 ± 24.14	83.33 ± 26.73	65.81 ± 35.22	76.86 ± 31.75	63.86 ± 37.77	62.97 ± 32.74	78.47 ± 28.13	67.64 ± 39.45
p	*0.013*	0.058	0.066	0.169	*0.004*	*< 0.001*	0.845	0.265	0.187	*0.006*	0.354	0.982
Stage												
Early	82.81 ± 25.44	82.41 ± 16.72	80.56 ± 23.34	80.56 ± 25.32	73.26 ± 26.20	77.78 ± 28.87	77.85 ± 27.75	82.74 ± 25.15	60.44 ± 42.46	61.78 ± 37.84	75.93 ± 32.14	72.89 ± 34.67
Advanced	68.15 ± 30.76	72.58 ± 22.04	67.26 ± 28.11	69.76 ± 30.41	63.52 ± 32.41	56.45 ± 35.63	62.40 ± 33.41	67.73 ± 36.27	56.44 ± 37.09	46.66 ± 27.45	73.79 ± 31.50	67.26 ± 37.96
p	*0.031*	0.050	*0.036*	0.115	0.191	*0.008*	0.038	0.084	0.583	*0.036*	0.702	0.555
Time since end of RT												
≤ 22 months	67.47 ± 29.06	73.89 ± 16.82	67.11 ± 25.99	70.56 ± 25.72	60.07 ± 31.56	57.78 ± 35.28	57.87 ± 32.96	61.49 ± 36.97	54.04 ± 35.12	45.09 ± 32.79	72.22 ± 30.26	63.78 ± 36.85
> 22 months	78.33 ± 29.96	77.22 ± 24.32	75.56 ± 27.95	76.11 ± 32.40	73.62 ± 28.95	68.89 ± 34.19	77.04 ± 29.22	82.20 ± 27.25	60.71 ± 41.67	58.49 ± 29.58	76.11 ± 32.84	74.11 ± 36.18
P	0.056	0.181	0.086	0.149	*0.026*	0.124	*0.004*	*0.004*	0.357	*0.039*	0.378	0.105
Trismus												
No	78.24 ± 28.65	78.57 ± 17.95	76.07 ± 24.06	80.36 ± 24.41	73.10 ± 24.75	75.00 ± 29.74	75.83 ± 30.90	76.95 ± 32.59	63.50 ± 36.74	59.52 ± 34.26	81.55 ± 25.93	78.62 ± 32.79
Yes	66.48 ± 30.47	72.16 ± 21.71	65.34 ± 29.14	65.34 ± 31.99	59.39 ± 34.50	52.27 ± 35.79	60.68 ± 33.23	66.68 ± 35.29	53.73 ± 38.93	43.82 ± 27.76	68.18 ± 34.25	58.16 ± 38.67
p	0.054	0.233	0.097	*0.027*	0.097	*0.003*	0.052	0.129	0.250	*0.021*	0.065	*0.009*
Hyposalivation												
No	82.50 ± 29.36	86.25 ± 15.12	77.50 ± 22.80	82.50 ± 28.21	83.40 ± 22.94	82.50 ± 24.47	76.70 ± 26.79	78.30 ± 29.29	80.00 ± 31.40	70.00 ± 28.53	77.50 ± 31.31	80.05 ± 33.15
Yes	70.01 ± 29.75	72.43 ± 21.22	70.51 ± 27.29	71.32 ± 29.06	62.47 ± 30.51	58.09 ± 35.21	66.72 ± 32.13	69.12 ± 35.25	50.94 ± 37.61	46.00 ± 30.61	72.79 ± 31.96	65.25 ± 37.55
p	0.073	*0.006*	0.335	0.095	*0.005*	*0.006*	0.241	0.320	*0.002*	*0.003*	0.576	0.084
Comorbidities												
No	75.26 ± 31.13	77.38 ± 21.95	79.76 ± 24.22	85.12 ± 21.43	69.36 ± 32.45	69.05 ± 29.12	69.07 ± 32.50	82.55 ± 27.83	63.50 ± 38.18	45.17 ± 29.42	78.57 ± 31.03	79.45 ± 29.49
Yes	70.83 ± 28.87	73.96 ± 19.95	63.96 ± 27.69	63.02 ± 31.37	64.65 ± 29.59	58.33 ± 39.05	66.04 ± 32.67	62.48 ± 36.22	52.02 ± 38.30	57.58 ± 32.91	70.31 ± 31.65	59.75 ± 41.27
p	0.381	0.308	*0.004*	*0.001*	0.291	0.230	0.636	*0.005*	0.163	0.076	0.127	*0.033*

Mann-Whitney test. $p < 0.05$

Table 4 Associations between total UW-QOL score and independent variables

Variables	Total UW-QOL score			*p***
	Crude MR (95% CI) lower/upper	*p**	Adjusted MR (95% CI) lower/upper	
Age				
< 62 years	1.0	*0.001*	1.0	*0.014*
≥ 62 years	1.25 (1.09–1.43)		1.17 (1.03–1.33)	
Location				
Mouth and oropharynx	1.0	*0.006*	1.0	0.635
Hypopharynx and larynx	1.18 (1.05–1.33)		1.03 (0.92–1.15)	
Stage				
Early	1.0	*0.005*	1.0	*0.016*
Advanced	0.84 (0.75–0.95)		0.89 (0.80–0.98)	
Time since end of RT				
≤ 22 months	1.0	*0.006*	1.0	0.122
> 22 months	1.19 (1.05–1.34)		1.09 (0.98–1.23)	
Hyposalivation				
No	1.0	*0.004*	1.0	*0.029*
Yes	0.83 (0.73–0.94)		0.88 (0.79–0.99)	
Trismus				
No	1.0	*0.001*	1.0	*0.002*
Yes	0.81 (0.72–0.92)		0.85 (0.77–0.94)	

*Crude and adjusted **Poisson regression model with robust variance; MR, mean ratio; CI confidence interval. $p < 0.05$

Trismus and hyposalivation were the main clinical oral variables associated with quality of life in the present study. Previous studies have also found that hyposalivation [24] and trismus [25] were associated with a negative impact on the quality of life of patients submitted to radiation for the treatment of head and neck cancer. In the present investigation, patients with trismus had a significantly poorer quality of life in both the crude and adjusted multivariate models. Scott et al. [21] found a strong association between trismus and both RT and advanced stages of the disease, specifically tumor size. Such findings explain the present results, as all patients had received 3-D conformal RT and more than two-thirds of the sample had tumors in the advanced stage.

In the bivariate analysis, trismus was significantly associated with the recreation, chewing, saliva, and anxiety subscales. The association with chewing may be explained by the fibrosis that occurs in muscle as a result of RT, which hinders eating and can cause nutritional problems [26]. Difficulty chewing can interfere with eating and social interactions, leading to weight loss, isolation, and depression [25], which may explain the associations with the recreation and anxiety subscales in the present study. Although the UW-QOL questionnaire is not specific to the psychological aspects of patients, the tool addresses the aforementioned domains, which have been associated with trismus, indirectly reflecting the association of recreation, anxiety and depression with a poorer quality of life.

Hyposalivation as a late-onset consequence of RT in survivors of head and neck cancer is a consensus in the literature [23]. However, few studies have compared this side effect to quality of life in patients having been submitted to RT. Most studies have only evaluated the subjective aspect (xerostomia) and not hyposalivation itself. The isolated evaluation of xerostomia is not necessarily an indicator of reduced salivary production [15]. In the present study, the adjusted multivariate analysis revealed an association between hyposalivation and quality of life. This association may be related to the discomfort caused by reduced salivary flow, with negative consequences for chewing, swallowing (dypshagia), and the sense of taste (dysgeusia). Previous studies have also found an association between hyposalivation and both dysgeusia [27] and dysphagia [28]. RT is believed to cause the loss of taste buds through the cytotoxic and anti-proliferative effect on irradiated tissues, leading to the loss of the sense of taste [29]. Both dysphagia and dysgeusia can result in weight loss and are associated with a negative impact on quality of life, which explains the strong association between hyposalivation and the chewing, swallowing, taste, and saliva subscales in the present study.

Patients with tumors located in the mouth and oropharynx had a poorer quality of life. Tumors in these locations can cause difficulties in breathing and swallowing and can compromise esthetics more in comparison to other locations in the

head and neck [7, 30]. Despite the strong association in the bivariate analysis and crude model of the multivariate analysis, this association lost its significance after the adjustment for confounding variables.

The saliva, taste, and chewing subscales on the UW-QOL had the lowest scores in the present study. This shows considerable coherence between the questionnaire and the clinical variables, as trismus and hyposalivation were the most significant clinical results, which directly reflect the most affected subscales. The UW-QOL has specific questions that refer to salivary flow, but not specifically to trismus, although we may indirectly associate trismus with chewing. Thus, the objective analysis of this study offers more accurate information regarding the association between trismus and quality of life. As trismus was associated with quality of life in the multivariate analysis, it may be important to evaluate this aspect objectively, rather than only collecting subjective information. Other results that demonstrate agreement were the subscales that the patients considered to be the most important in the 7 days prior to the administration of the questionnaire (saliva, pain, and speech), which were also strongly related to the results of the adjusted model of the multivariate analysis. The UW-QOL is a screening tool that has merit, but clinicians should be aware that its simplicity may lead to the loss of information from some patients and that the details of their problems may be lost [31].

The present study has limitations that should be considered. As the investigation had a cross-sectional design, it was not possible to compare the UW-QOL to previous results or to a control group. However, comparing the findings with the results of previous studies, the means of the subscales were similar to those reported for groups of patients with neoplasms, although studies involving patients having been submitted to intensity-modulated radiotherapy (IMRT) report higher mean quality of life scores [32, 33]. This technique is recognized as being less harmful to the patient and causing fewer side effects compared to 3D-conformal RT, consequently exerting less of an impact on quality of life [34, 35]. Despite the consensus in the literature on the benefits of IMRT, 3D-conformal RT is still widely used in Brazil, especially in the public sector, due to financial constraints. Indeed, all patients in the present sample received 3D-conformal RT, which is one of the possible explanations for the results encountered. The present study also did not evaluate the range of motion of the shoulder and neck objectively. However, the UW-QOL questionnaire addresses this variable subjectively through the domain shoulder. In the bivariate analysis, patients who had completed the treatment more than 22 months earlier had higher mean UW-QOL scores in this domain, indicating a better quality of life, which is in agreement with data from previous studies in the literature [36].

Sociodemographic factors can exert an influence on quality of life [37]. Moreover, a higher incidence of head and neck cancer is associated with low socioeconomic status [38]. In the present study, educational level was used as the indicator of socioeconomic status (schooling variable). As nearly the entire sample consisted of patients with a low level of education, no relevant differences in quality of life were found in relation to this variable.

The present findings may be valid for similar populations and offer knowledge on how younger patient age, advance tumor staging, presence of trismus, and hyposalivation are associated with quality of life of head and neck oncological patients. These findings can assist in the development of public health strategies and the planning of supportive care for patients having undergone treatment for head and neck cancer with the aim of preventing and/or reducing post-treatment harm, thereby improving the quality of life of these patients. Although the importance of such measures is known, it is not easy to translate evidence generated in the literature to effective application in clinical practice. This raises issues related to technical resources, human resources, and interdisciplinary teamwork [39].

Conclusion

Survivors of squamous cell carcinoma of the mouth oropharynx, hypopharynx, or larynx experience a negative impact on quality of life that is strongly associated with presence of trismus, hyposalivation, advanced stage tumors, and a younger age. These findings suggest that a specific approach focused on these aspects is important to the promotion of better quality of life for such patients in the long term.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no conflict of interest.

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