

Changes in health related quality of life in women and men undergoing radiation treatment for head and neck cancer and the impact of smoking status in the radiation treatment period.

Helen Egestad and Nina Emaus

Faculty of Health Sciences, Department of Health and Care Sciences, UiT, The Arctic University of Norway, 9037 Tromsø, Norway

Abstract:

Purpose The aim of this study was to evaluate health-related quality of life (HRQOL) in women and men undergoing radiation treatment for head and neck cancer through the intervention period and examine if age, body mass index (BMI) and smoking status at baseline may modify changes in HRQOL.

Methods HRQOL was examined by the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the EORTC QLQ-H&N35, in the beginning and end of the treatment period in 65 patients at the University Hospital in Northern Norway. Changes in HRQOL were calculated and compared by paired sample T-tests. Linear multiple regression analyses were used to examine if baseline characteristics had any influence HRQOL changes.

Results Most aspects of HRQOL declined substantially and significantly ($p < 0.001$) with a magnitude of more than one standard deviation during the radiation treatment period irrespective of sex and age. Smoking status at baseline had some, albeit minor, influence on changes in HRQOL. Patients who continued smoking during therapy had significantly higher decline in several aspects of HRQOL, compared to patients who stopped smoking.

Conclusions HRQOL decline with substantial magnitude in patients undergoing radiation treatment for head and neck cancer, but smoking cessation may modify the declining quality of life.

Introduction

Treatments of head and neck (H&N) cancer include surgery, radiotherapy (RT), chemotherapy, target therapy or a combination of these modalities. The diagnosis and the following treatment may exert a severe impact on patient's quality of life (QOL) (So et al., 2012). The malignancy affects the most visible area of the body, and may influence the most

fundamental activities of daily life in a negative way, such as speech, breathing, eating and drinking (Larsson and Hedelin, 2003; Wells 1998). H&N cancer patients' illness often involves physical symptoms, psychological distress, as well as side effects from RT (Archer et al., 2008). The treatment can result in dry mouth (xerostomia), oral discomfort, mucositis, recurrent microbial infections, difficulty in chewing and swallowing, increased incidence of dental caries, impaired taste, and an inability to wear dentures (Parsons et al., 1994). In addition, depression is reported to increase in H&N cancer patients undergoing RT (Neilson et al., 2010; Kelly et al., 2007).

The interest in health-related quality of life (HRQOL) (i.e. the physical, mental, and social functioning and well-being) in H&N cancer patients has increased over the two decades (So et al., 2012). Even if the most important outcome for cancer patients is overall survival, the disease and its treatment often have a major impact on HRQOL and functional status (List et al., 2002). Reliable and valid HRQOL questionnaires are available (Aaronson et al., 1993; Bjordal et al., 2000; Ringash and Bezjak, 2001). The EORTC QLQ-H&N35 is widely used to measure quality of life in H&N cancer patients (Singer et al., 2013). Both prospective and cross-sectional studies (Bjordal et al., 2001; Hammerlid et al., 2001a, 2001b, 2001c; Nguyen et al., 2002; Talmi et al., 2002; Shepherd and Fisher, 2004) have documented reductions in HRQOL in populations of H&N cancer patients who have received RT. Several studies have also examined changes in HRQOL during the treatment period (Bjordal et al., 2001; Henson et al., 2001; Airolli et al., 2004; Parliament et al., 2004; Jabbari et al., 2005; Braam et al., 2007; Curran et al., 2007; Ackerstaff et al., 2009; Ackerstaff et al., 2012; Maguire et al., 2011; Maurer et al., 2011; Nutting et al., 2011). These studies show that QOL worsens during treatment and improves after cessation of treatment, returning to baseline QOL by 12 months after treatment (So et al., 2012; Curran et al., 2007; Bjordal et al., 2001). During the radiation treatment period a number of functions and symptoms change significantly, but a direct comparison between studies is difficult because of the varying design and HRQOL measurements. There are also contradictory findings about the gender influence on QOL before and after treatment (So et al., 2012). According to Bjordal et al. (2001) women scored lower than men at baseline. Bozec (2008), on the other hand found that women had fewer or less severe general and H&N symptoms 12 months after surgery, particularly concerning dyspnoea and sticky saliva. de Graeff et al. (2000) found that women scored lower on fatigue, pain, physical and emotional functioning and role activities, social contacts and social eating 6 and 12 months after treatment. Scrimger et al. (2007) who investigated the correlation

between saliva flow rates and various toxicity endpoints commonly used in H&N cancer treatment, demonstrated higher improvement in women than in men from pre-treatment to 12 months post-treatment, and patients who never had smoked had higher QOL scores before and after treatment than ex-smokers and current smokers (Scrimger et al., 2007). The influence of smoking on side effects in H&N cancer patients has rarely been studied (Jensen et al., 2007). Ronis et al. (2008) found that smoking was highly predictive of poorer QOL scores at 12 months for most items. On the other hand, Aarstad et al. (2007) found no significant association between rate of cigarette smoking and levels of general coping in patients who had been disease-free for at least 1 year.

Although many studies have focused on survival rates and QOL in patients with H&N cancer, the effort has primarily focused on improving treatment techniques or use of therapies or combined modalities (So et al., 2012). To be able to improve supportive care, we need more knowledge on factors influencing HRQOL in this vulnerable patient group. This paper focuses on the HRQOL and functional status of a representative sample of H&N cancer patients from the start to the end of the radiation treatment period. The purpose of the current study was twofold. First, the aim was to examine women`s and men`s HRQOL during radiation treatment. Secondly, the aim was to examine if smoking status had any impact on head and neck cancer patients` HRQOL during radiation treatment.

Methods

Study design and participants

The study was conducted at the University Hospital in Northern Norway, in a period from May 2009 to November 2012. All adults patients (18 years or older) with a primary H&N cancer, referred to the oncology center for radiotherapy, were consecutively invited to participate in the study. When the referral arrived at the department, the chief radiation therapist informed the research assistants, all radiation therapists, working in the department. The research assistants approached eligible patients, explained the consent and considered whether the patients were able to complete the questionnaires and collected the data. Patients who were unable to answer the HRQOL questionnaires as a result of mental disturbance, or unable to fill the questionnaire for other reasons, or if they were unable to speak and understand Norwegian, were excluded. Each eligible patient received a letter broadly explaining the purpose and the methods of the study and the level of commitment required to participate in the project. Eighty patients met the criteria and were invited to participate in the

study. Three patients refused participation and one relative of a patient declined. Eleven patients did not return the written consent. Sixty-five were included, resulting in a recruitment rate of 81 %. The study was approved by the Regional Committee for Medical Research Ethics (REK NORD 200900504-3KST017/400), and the Norwegian Social Science Data Services (21831).

Data collection

Socio demographic and tumor-related patient characteristics were recorded at inclusion, i.e. sex, age, residence, tumor location according to ICD-10, TNM (T=tumor size, N=node, M=metastasis) and planned treatment was noted. In addition, a study-specific questionnaire was filled out by the radiation therapist. The patients also responded to whether they smoked, had smoked earlier or stopped smoking after diagnosis.

HRQOL questionnaires

Data were collected at two time points: at baseline which was the first radiation treatment week; (T1), and in the last week, after 60 Gy; (T2). At T1 and T2, the patients filled in the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 (Aaronson et al 1993) and EORTC QLQ-H&N35 (Bjordal et al. 2001). The EORTC QLQ-C30 questionnaire is a generic questionnaire developed for patients with any cancer type. The questionnaire is designed for self-administration and assesses multiple dimensions of HRQOL and responses to this 30-item questionnaire are categorized into five functional domains (physical, role, emotional, cognitive, and social) (scored on a four-point scale), one global HRQOL domain (scored on a seven-point scale), three symptom domains (fatigue, nausea/vomiting, pain) and six single items (scored on a four-point scale). Each score is transformed into 0-100 point scale. EORTC QLQ-H&N35 is a questionnaire specifically developed for H&N cancer patients consisting of 35 items on HRQOL. It includes seven scales (pain, swallowing, senses, speech, social eating, social contact and sexuality) and 11 single items (problems with teeth, problems opening the mouth, dry mouth, sticky saliva, cough, feeling ill, pain killers, nutritional supplements, feeding tube, weight loss and weight gain). Items 1-30 are scored on a four-point scale (1; not at all, 2; a little, 3; quite a bit, 4; very much). Items 31-35 have a yes (2) or no (1) response format. Both EORTC instruments were scored according to recommendations in the EORTC QLQ-C30 scoring manual (Borggreven et al., 2007). In the five functional scales and the global HRQOL scale, a high score

represents a high level of functioning or global HRQOL. In the symptom scales and single items, a higher score implies a high level of symptoms or problems.

Clinical treatment

RT was administered to the primary tumor and the regional neck lymphatics (dependent on N stage) by conventional fractionation, i.e. dose of 2 Gy, 1 fraction per day, 5 days per week. The total radiation doses were 60-70 Gy. RT was delivered using megavoltage equipment (6MV linear accelerator) in general over a period of six to seven weeks. In all patients, planning computed tomography scans were used, and all patients were treated with three-dimensional conformal or intensity-modulated RT. None of the patients had distant metastases.

Statistical analysis

Baseline characteristics, distribution of tumor location, tumor stage and nodal stage were compared between women and men using chi square testing for categorical variables and Independent sample T-Tests for continuous variables. The mean scores with the standard deviation (SD) of each item are presented at baseline and at the end of the treatment period. Differences in scores were calculated by subtraction of scores from baseline to end of treatment, and score differences are presented as mean differences (SD). Differences in mean score between baseline and end were compared using Paired Sample T-test, and differences in scores between the sexes were compared using Independent sample T- tests. To examine if factors present at baseline influenced HRQL during the treatment period, linear multiple regression analyses were applied using the difference in HRQL score as dependent variable and the baseline variables age, body mass index (BMI), smoking status (yes-no), first in univariate analyses. The variables which were significant predictors in these analyses, including BMI, were included in an initial multivariable model. In the final model only the significant variables were included. The significance level was set at $P < 0.05$ using the statistical software SPSS 21.0 for Windows.

Results

The majority of patients were treated with surgery before they received RT, and 34% were treated with cisplatin (chemotherapy) in addition to RT. The majority of the patients received RT as 2 Gy-per-fraction, 5 days-a-week to a total dose of 64 to 70 Gy. The baseline characteristics of the patients are presented in Table 1. The mean age was 62 (10.5) years in

men and 53.5 (12.9) years in women ($p=0.01$). Men were heavier, weighted more than women, but BMI and smoking status were not different between the sexes. Dividing the tumor locations into four groups (oral cavity, pharynx, larynx, and other), the most common sites of primary tumor were the pharynx and the larynx, followed by the oral cavity (Table 2). There were 15 men with pharynx, 14 men with larynx and 12 with oral cavity tumors and the corresponding tumors in women were five pharynx, one larynx and six oral cavity, respectively. Squamous cell carcinoma was evident in 89 % of the participants (data not shown). With regard to the T-stage, 39 (60%) had T1 and T2, 26 (40%) had NO. Lymph node status had a similar distribution in both sexes (Table 2).

At baseline, there were no significant differences between women and men concerning any HRQOL item, either in the EORTC-C30 (Table 3) or the EORTC-QLQ-H&N35 (Table 4) ($p>0.127$) (Independent sample T-Tests). At the end of treatment period, there were still no differences between the sexes for any item, except for role functioning (EORTC-C30) where women scored lower than men, although the difference was of borderline significance ($p>0.049$) (Table 3) (Independent sample T-Tests). During the treatment period, most item scores in the EORTC-C30 declined significantly (Paired Sample T-test), except emotional and social function in women (Table 3). In the single item questions of EORTC-C30, there were significant changes in the appetite and constipation scores in both genders during the treatment period (Table 3), but no significant changes in dyspnea, insomnia and diarrhea (Table 3). In the EORTC-QLQ-H&N35, men's scores for all items deteriorated during treatment. Women's scores worsened for all symptoms except weight gain (which illustrated that a minority of patients put on weight during treatment), sexuality, teeth problems and coughing (Table 4). The only significant change in scores during treatment between men and women was in relation to insomnia, where women's scores changed more than men's ($p=0.012$) (symptom score QLQ-C30) (Independent sample T-Tests). Pain scores also tended to increase more in women compared to men ($p=0.053$) (specific QLQ-H&N35). When adjusting for age, these changes were however no longer significantly different, insomnia; $p=0.332$ and pain; $p=0.834$. The only item that was significantly different between the sexes after age adjustment was self-reported weight loss which was more frequently reported by women ($p=0.024$).

Because of the similar changes in HRQOL in women and men during the treatment period, we did not stratify or adjust for sex in further analyses. In bivariate regression analyses, there was a significant association between age and changes in the EORTC QLQ H&N35 single

item open mouth ($p=0.024$) (Table 5). BMI was not associated with any item, but smoking status was associated with use of pain killers ($p=0.043$) (specific QLQ H&N35) and was of borderline significance for social eating ($p=0.055$) (specific QLQ H&N35) (Table 5).

The variables which were significant predictors in the bivariate analyses (smoking status and age) were used as independent variables and the differences in HRQL scores as dependent variables in further multivariable modelling. The final models indicated that smoking status was associated with increased fatigue ($p=0.027$), pain ($p=0.009$) (symptom score QLQ-C30), speech ($p=0.017$) (specific QLQ-H&N35) and maximum mouth opening (single-item QLQ-H&N35) (Table 5). In addition, smoking status was also associated with poorer cognitive function ($p=0.041$). Age was furthermore negatively associated with pain ($p=0.042$) (symptom score QLQ-C30), maximum mouth opening ($p=0.006$) and use of feeding tube ($p=0.046$) (single-item QLQ-H&N35).

Discussion

In the present study we evaluated changes in HRQOL and examined if factors present at baseline modified these changes during radiation treatment in a population of 65 H&N cancer patients. Most aspects of HRQOL declined significantly during the radiation treatment period in both sexes, a finding which is in accordance with other studies (Bjordal et al., 2001; Curran et al., 2007; Airolidi et al., 2004; Braam et al., 2007; Akerstaff et al., 2009; Akerstaff et al., 2012; Shepherd and Fisher, 2004). In principle, there were no differences in reported HRQOL between the sexes at baseline and at the end of the treatment period, except that at the end of the treatment period women scored lower than men in role functioning, as also reported by de Graeff et al. (2000). This result can possibly be related to the fact that women in our study were younger (mean age 53.5 years) than men and thereby may have been more affected in their role functioning.

Among factors present at baseline, smoking status had some impact on changes in HRQOL. Patients who continued smoking through the intervention period had poorer QOL compared to never smokers and those who quit smoking. To our knowledge, this is the first study to demonstrate a relationship between continued smoking and QOL during the radiation treatment period. Continued smoking was associated with higher decline in several aspects of HRQOL, except for cognitive function, where smokers had better QOL than patients who did not smoke. This finding can be seen in the context of the fact that nicotine may improve performance in relation to attention and memory (Rezvani and Levin 2001). Former smokers

who had stopped smoking before radiation treatment, reported better HRQOL, and the lowest HRQOL deterioration was found in patients who never had smoked. This result was also reflected in the study by Jensen et al. (2007) who found that smoking after radiotherapy or surgery in H&N cancer patients adversely influenced a wide range of QOL endpoints. In their study, quitters had better HRQOL than patients who continued to smoke after treatment, and previous smokers` HRQOL scores fell between those of never smokers and continuous smokers (Jensen et al., 2007). The link between tobacco smoking and H&N cancer has been highlighted by others: Smoking during RT can reduce its efficacy (Meyer et al., 2008; Browman et al., 1993) and Edwards (2004), and Browman et al. (2002) showed better survival in light smokers compared to moderate and heavy smokers. Humphris and Rogers (2004) examined the association of smoking and anxiety in oral cancer patients after treatment and found that past and current smoking behaviour was associated with psychological distress (Humphris and Rogers 2004). Ronis et al. (2008) focused on QOL in patients with head and neck cancer shortly before treatment and found that smoking was a major predictor of poor QOL. Aarstad et al. (2007) found significant correlations between the number of cigarettes smoked per week and QOL in head and neck cancer after treatment. During radiation treatment a significant correlation was shown with smoking and the volume of mucosa irradiated (Rugg et al., 1990) and smoking increased the severity of mucositis and acute skin reactions (Porock et al., 2004). Wells et al (2004) found that head and neck cancer patients who continued smoking during RT were more likely to develop skin reactions than former smokers and non-smokers. Non-smokers had lower skin toxicity scores (Wells et al. 2004). Sharp et al. (2013) examined risk factors for severe acute radiation skin reactions in women undergoing RT for breast cancer. Radiation dose and smoking were the factors most strongly related to severe acute skin reactions (Sharp et al. 2013). Duffy et al. (2002) who used a QOL questionnaire SF-36V (Ware et al., 1994) on 81 head and neck cancer patients found that smoking was negatively associated with physical and social functioning, general health, vitality, and role-emotional health. Although different in design and measurements, these findings are all comparable with ours.

The data presented here, illustrate how a number of functions and symptoms change significantly during the radiation treatment period, particularly influencing mouth opening, speech problems, pain, fatigue, use of feeding tube and use of pain killers. Changes in HRQOL were also analyzed with regard to the background variables sex, age and BMI. Sex did not influence the observed changes in HRQOL in this population, but older patients

reported more pain, more use of pain killers and more problems with mouth opening. Sex was not a significant factor in a study by de Graeff et al. (2000), but age had an influence on fatigue, physical functioning, social eating, and speech; as older patients had worse scores. Williamson et al. (2011) found no evidence of an age effect when they evaluated HRQOL of patients with head and neck cancer, but they did not include sex analyses in their study. HRQOL was associated with patients' age in Lòpez-Jornets et al. study (2012), who evaluated 94 patients undergoing treatment for head and neck cancer in Spain. In their study females had a slight tendency to score worse than males for some functioning scales with symptoms, financial difficulty and sexuality. Hammerlid et al. (2001a) found that females scored worse than males for some areas at diagnosis, in particular, in emotional functioning. These conflicting results on gender differences cannot easily be explained, but overall, gender does not seem to have a major influence on HRQL during radiation treatment – the decline seems to be similar in the two sexes.

There are strengths and weaknesses to be discussed in the present study. The socio-demographic characteristics of the sample are representative of head and neck populations with a preponderance of men (75.4%). Among eligible patients, 81% agreed to participate in the study. The study cohort is therefore likely to be a representative sample of this patient group. A weakness of the study is that we did not examine the participants' physical condition, nutrition status and morbidity at baseline. We were not able to repeat the examination during the treatment period, so we do not know when the decline in HRQOL started. It is also a limitation to our study that we were not able to follow the cohort after cessation of treatment. Therefore, we do not know if HRQOL improved after the end of treatment. What we know is that the 5-year survival rate of these patients is 65.9% (Pulte and Brenner, 2010) and that HRQOL declines substantially during RT. The sample size should have been larger particularly for the regression analysis therefore our findings must be interpreted with caution. Another weakness in this study is that patients who said they had given up smoking may in fact still be smokers. According to Hald et al. (2003), recent quitters may under-report their current smoking status. Furthermore, we do not know the length of nicotine abstinence in this population. However, all data were collected in structured interviews and all patients answered the questions about tobacco use with a research assistant present.

Implications for practice include the need for health care providers to be aware of the impact that continued smoking during RT has on patients HRQOL. Before treatment starts, patients

should be advised that continued smoking is associated with greater decline in quality of life. Radiation therapists and nurses should provide smoking cessation support prior to, during and at the end of the 5-7 week RT treatment period. Psychological support during treatment is important for all patients but perhaps more for smokers trying to quit as there is an emotional burden to smoking cessation in addition to the burden of having cancer and undergoing treatment.

Conclusions

HRQOL is severely affected during treatment for head and neck cancer patients, independent of patients` gender, age and BMI. In this study, smoking status at baseline was the only factor which seemed to influence the magnitude of HRQOL loss. Head and neck cancer patients who quit smoking before treatment may reduce the decline in their quality of life. Radiation therapists and nurses should therefore provide greater levels of smoking cessation support to patients before they start their treatment.

Conflicts of interest

The authors have no funding or conflicts of interest to disclose.

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Table 1 Patient characteristics at baseline (n=65)

Characteristics	Women (n=16)	Men (n=49)	P-value
Age (years) mean (SD)	53.5 (12.9)	62 (10.5)	0.010
Height (cm) mean (SD)	164.3 (6.7)	178.8 (6.8)	<0.001
Weight (kg) mean (SD)	67.2 (13.9)	83.1(12.2)	<0.001
BMI (kg/m ²) mean (SD)	1.6 (5.6)	1.4 (5.7)	0.287
Smoker (n/%)	4 (25%)	9 (18%)	0.559
Never smoker	5 (31%)	11(22%)	
Former smoker	7 (44%)	29 (60%)	

Table 2 Pretreatment characteristics of the study cohort (n=65)

Characteristics	Women % (n)	Men % (n)
Tumor location		
Oral cavity	37.5 (6)	24.5 (12)
Pharynx	31.2 (5)	30.6 (15)
Larynx	6.3 (1)	28.6 (14)
Others/unknown	25.0 (4)	16.3 (8)
T-stage		
T1	56.3 (9)	22.4 (11)
T2	12.5 (2)	34.7 (17)
T3	12.5 (2)	12.2 (6)
T4	6.3 (1)	14.3 (7)
Tx		4.1 (2)
Not stated	12.5 (2)	12.2 (6)
N-stage		
N0	43.8 (7)	38.8 (19)
N1	25.0 (4)	26.5 (13)
N2	12.5 (2)	18.4 (9)
Not stated	18.7 (3)	16.3 (8)

Table 3 Development in quality of life (EORTC-C30) from baseline to end of treatment

EORTC QLQ-C30	Baseline Mean (SD)	End Mean (SD)	Mean difference (SD)	P-value
Functional scales				
Physical functioning				
Men	82.8 (17.2) (n=48)	68.2(24.6) (n=44)	15,9;20,2	0.000
Women	83.3(13.5) (n=14)	65.0(19.1) (n=12)	20,6;21,2	0.006
Role functioning				
Men	73.6(27.5) (n=48)	48.3(34.6) (n=40)	26,5;31,7	0.000
Women	65.5(22.1) (n=14)	26.4(27.0) (n=12)	43,1;20,7	0.000
Emotional functioning				
Men	84.3(19.1) (n=48)	74.4(24.0) (n=44)	10,1;27,6	0.021
Women	75.6(27.0) (n=14)	77.1(20.8) (n=12)	-1,4;24,1	0.845
Cognitive functioning				
Men	86.8(19.4) (n=48)	74.1(26.5) (n=44)	13,4;23,2	0.000
Women	84.5(20.1) (n=14)	65.3(36.6) (n=12)	20,8;31,9	0.045
Social functioning				
Men	73.6(27.3) (n=48)	62.7(31.0) (n=42)	10,6;20,3	0.002
Women	65.5(30.3) (n=14)	48.6(34.4) (n=12)	20,8;46,1	0.146
Global health scale				
Men	67.7(20.4) (n=48)	48.3(25.8) (n=44)	20,3;20,3	0.000
Women	61.3(29.5) (n=14)	45.1(21.7) (n=12)	22,9;29,5	0.021
Symptom scale				
Fatigue				
Men	32.2(22.4)(n=48)	56.6(27.8) (n=44)	-24,8;23,0	0.000
Women	38.9(28.8) (n=14)	61.1(29.8) (n=12)	-25,9;31,5	0.016
Nausea and vomiting				
Men	14.1(23.1) (n=48)	29.9(30.6) (n=44)	-14,9;33,2	0.005
Women	17.9(21.1) (n=14)	34.7(29.7) (n=12)	-20,8;23,7	0.011
Pain				
Men	16.7(21.2) (n=48)	49.2(32.5) (n=44)	-33,3;28,4	0.000
Women	21.4(20.1) (n=14)	52.8(34.7) (n=12)	-34,7;38,6	0.010
Single-item question				

Dyspnoea				
Men	23.6(24.8) (n=48)	29.5(28.0) (n=44)	-6,2;24,4	0.103
Women	14.3(21.5) (n=14)	19.4(22.3) (n=12)	-11,1;21,7	0.104
Insomnia				
Men	27.8(29.4) (n=48)	32.6(31.7) (n=44)	-4,6;25,8	0.243
Women	42.9(40.1) (n=14)	25.0(25.1) (n=12)	19,4;36,1	0.089
Loss of appetite				
Men	19.4(31.4) (n=48)	63.6(36.5) (n=44)	-43,4;36,8	0.000
Women	33.3(39.2) (n=14)	60.6(32.7) (n=11)	-33,3;36,5	0.013
Constipation				
Men	20.1(23.6) (n=48)	46.2(38.2) (n=44)	-27,9;44,2	0.000
Women	20.5(34.8) (n=13)	50.0(41.4) (n=12)	-39,4;44,3	0.014
Diarrhea				
Men	17.0(24.9) (n=47)	18.2(28.3) (n=44)	0,0;32,9	1.0
Women	9.5(20.4) (n=14)	9.1(15.6) (n=11)	3,0;18,0	0.588
Financial difficulty				
Men	18.1(30.7) (n=48)	25.0(32.2) (n=44)	-6,2;31,9	0.210
Women	19.0(28.4) (n=14)	9.1(15.6) (n=11)	6,1;20,1	0.341

Table 4 Development in quality of life (EORTC-QLQ-H&N35) from baseline to end of treatment in women and men

EORTC QLQ-H&N35	Baseline Mean (SD)	End Mean (SD)	Mean difference (SD)	P-value
Pain				
Men	18.7 (17.1) (n=49)	47.0(27.4) (n=44)	-29,2;24,2	0.000
Women	19.0(14.4) (n=14)	62.5(24.2) (n=12)	-45,1;27,2	0.000
Swallowing				
Men	10.8(14.7) (n=49)	45.7(28.3) (n=43)	-34,2;31,5	0.000
Women	8.3(16.0) (n=14)	43.7(33.5) (n=12)	-40,3;34,1	0.002
Senses				
Men	21.1(29.6) (n=49)	51.9(31.4) (n=44)	-31,4;32,0	0.000
Women	21.4(20.1) (n=14)	56.9(25.1) (n=12)	-38,9;27,8	0.001
Speech				
Men	19.7(18.9) (n=49)	45.3(29.5) (n=43)	-24,7;28,7	0.000
Women	11.9(23.7) (n=14)	37.0(24.3) (n=12)	-30,6;20,2	0.000
Social eating				
Men	16.1(20.5) (n=49)	49.8(28.0) (n=43)	-35,1;30,3	0.000
Women	16.1(21.3) (n=14)	50.8(24.3) (n=11)	-39,4;18,3	0.000
Social contact				
Men	4.7(8.0) (n=48)	23.9(26.8) (n=41)	-19,0;26,5	0.000
Women	6.7(11.4) (n=14)	32.7(26.1) (n=11)	-24,8;20,5	0.002
Sexuality				
Men	29.3(30.6)(n=44)	47.7(32.2) (n=37)	-23,0;38,9	0.002
Women	43.9(34.4) (n=11)	60.7(40.4) (n=10)	-16,7;41,8	0.296
Single-item questions				
Teeth				
Men	10.6(25.2) (n=47)	18.3(29.6) (n=42)	-8,9;23,6	0.020
Women	2.4(8.9) (n=14)	25.6(13.0) (n=12)	-2,8;9,6	0.339
Dry mouth				
Men	37.4(30.9) (n=49)	65.9(30.4) (n=43)	-28,7;30,5	0.000
Women	38.1(31.6) (n=14)	63.9(33.2) (n=12)	-30,6;36,1	0.014

Sticky saliva				
Men	33.3(30.9) (n=48)	69.8(31.9) (n=42)	-37,3;33,1	0.000
Women	31.0(27.6) (n=14)	75.0(32.2) (n=12)	-50,0;33,3	0.000
Coughing				
Men	23.8(20.4) (n=49)	43.4(29.6) (n=43)	-19,4;26,5	0.000
Women	19.0(28.4) (n=14)	27.8(23.9) (n=12)	-13,9;30,0	0.137
Maximum mouth opening				
Men	19.7(27.1) (n=49)	41.1(35.5) (n=43)	-20,9;33,4	0.000
Women	11.9(28.1) (n=14)	47.2(33.2) (n=12)	-33,3;34,8	0.007
Weight loss				
Men	24.5(43.4) (n=49)	61.9(49.2) (n=42)	-40,5;49,7	0.000
Women	15.4(37.6) (n=13)	75.0(45.2) (n=12)	66,7;49,2	0.001
Weight gain				
Men	38.3(49.1) (n=47)	5.0(22.1) (n=40)	33,4;53,0	0.000
Women	23.1(43.9) (n=13)	9.1(30.2) (n=11)	18,2;60,3	0.341
Use of nutritional supplements				
Men	22.4(4.,2) (n=49)	60.5(49.5) (n=43)	-39,5;49,5	0.000
Women	15.4(37.6) (n=13)	50.0(52.2) (n=12)	-45,5;52,2	0.016
Use of feeding tube				
Men	4.3(20.4) (n=47)	37.2(48.9) (n=43)	-16,3;57,4	0.000
Women	7.1(26.7) (n=14)	50.0(52.2) (n=12)	-45,5;52,2	0.007
Use of pain killers				
Men	42.9(50.0) (n=49)	93.0(25.8) (n=43)	-48,8;50,6	0.000
Women	57.1(51.4) (n=14)	83.3(38.9) (n=12)	-33,3;49,2	0.039
Feeling ill				
Men	17.9(22.9) (n=49)	45.2(29.3) (n=42)	-29,1;28,7	0.000
Women	23.8(24.2) (n=14)	47.2(36.1) (n=12)	-27,8;31,2	0.010

Table 5 The effect of age, body mass index (BMI) and smoking on HQRL changes in patients undergoing radiation therapy

HRQL	Univariate regression analyses			Multivariate regression analyses		
	Age	BMI	Smoking	Age	BMI	Smoking
EORTC QLQ-C30	p-value	p-value	p-value	p-value	p-value	p-value
Functional scales						
Physical diff	0.383	0.112	0.083	0.728	0.072	0.116
Role diff	0.691	0.358	0.668	0.421	0.320	0.424
Emotional diff	0.186	0.484	0.677	0.292	0.454	0.735
Cognitive diff	0.580	0.170	0.125	0.155	0.100	0.041
Social diff	0.252	0.658	0.273	0.245	0.738	0.361
Global health diff	0.529	0.615	0.655	0.354	0.678	0.474
Symptom scale						
Fatigue	0.912	0.117	0.074	0.411	0.061	0.027
Nausea and vomiting	0.663	0.431	0.511	0.333	0.530	0.195
Pain	0.293	0.611	0.060	0.042	0.390	0.009
Dyspnoea	0.569	0.327	0.852	0.748	0.333	0.935
Insomnia	0.903	0.406	0.655	0.721	0.466	0.502
Loss of appetite	0.896	0.486	0.265	0.647	0.588	0.276
Constipation	0.690	0.913	0.985	0.698	0.846	0.588
Diarrhea	0.151	0.855	0.303	0.157	0.804	0.767
Financial difficulty	0.679	0.468	0.411	0.448	0.404	0.332
EORTC QLQ-H&N35						
Pain	0.644	0.920	0.445	0.429	0.828	0.336
Swallowing	0.181	0.313	0.080	0.057	0.410	0.080
Senses	0.967	0.537	0.748	0.996	0.559	0.891
Speech	0.301	0.911	0.078	0.067	0.674	0.017
Social eating	0.758	0.603	0.055	0.340	0.782	0.064
Social contact	0.192	0.397	0.250	0.099	0.308	0.137
Sexuality	0.492	0.318	0.505	0.242	0.212	0.204

Single-item questions						
Teeth	0.878	0.617	0.217	0.749	0.528	0.231
Dry mouth	0.452	0.174	0.101	0.773	0.228	0.254
Sticky saliva	0.363	0.587	0.076	0.598	0.698	0.216
Cough	0.675	0.213	0.412	0.379	0.157	0.149
Maximum mouth opening	0.024	0.799	0.356	0.006	0.608	0.049
Weight loss	0.170	0.517	0.951	0.255	0.513	0.926
Weight gain	0.833	0.506	0.666	0.887	0.513	0.969
Use of nutritional supplements	0.763	0.204	0.145	0.761	0.408	0.079
Use of feeding tube	0.213	0.658	0.176	0.046	0.920	0.058
Use of pain killers	0.490	0.901	0.043	0.154	0.673	0.021
Feeling ill	0.267	0.998	0.846	0.142	0.967	0.690