

Residual deficits in quality of life one year after intensity-modulated radiotherapy for patients with locally advanced head and neck cancer

Results of a prospective study

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Abstract

Purpose Patients with locally advanced head and neck cancer (LAHNC) undergo life-changing treatments that can seriously affect quality of life (QoL). This prospective study examined the key QoL domains during the first year after intensity-modulated radiotherapy (IMRT) and identified predictors of these changes in order to improve patient outcomes.

Patients and methods A consecutive series of patients with LAHNC completed the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core module (QLQ-C30) and the HNC-specific QLQ-HN35 before (t0) and at the end (t1) of definitive or adjuvant IMRT, then at 6–8 weeks (t2), 6 months (t3), and 1 year (t4) after IMRT.

Results Patients ($n=111$) completing questionnaires at all five time points were included (baseline response rate: 99%; dropout rate between t0 and t4: 5%). QoL deteriorated

in all domains during IMRT and improved slowly during the first year thereafter. Many domains recovered to baseline values after 1 year but problems with smelling and tasting, dry mouth, and sticky saliva remained issues at this time. Increases in problems with sticky saliva were greater after 1 year in patients with definitive versus adjuvant IMRT ($F=3.5$, $P=0.05$).

Conclusion QoL in patients with LAHNC receiving IMRT takes approximately 1 year to return to baseline; some domains remain compromised after 1 year. Although IMRT aims to maintain function and QoL, patients experience long-term dry mouth and sticky saliva, particularly following definitive IMRT. Patients should be counseled at the start of therapy to reduce disappointment with the pace of recovery.

Keywords Rehabilitation · Xerostomia · Toxicity · Taste sense · Sense of smell

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Residuale Defizite in der Lebensqualität ein Jahr nach intensitätsmodulierter Strahlentherapie bei Patienten mit lokal fortgeschrittenen Kopf-Hals-Tumoren

Ergebnisse einer prospektiven Studie

Zusammenfassung

Hintergrund Die Therapie von Patienten mit lokal fortgeschrittenen Kopf-Hals-Tumoren (LFKHT) geht mit einschneidenden Veränderungen einher und beeinflusst die Lebensqualität (LQ) erheblich. Diese prospektive Studie untersucht die LQ während des ersten Jahres nach intensitätsmodulierter Strahlentherapie (IMRT) und hat Prädiktoren dieser Veränderungen herausgearbeitet, um Therapieergebnisse verbessern zu können.

Patienten und Methoden Patienten mit LFKHT füllten Lebensqualitätsfragebögen der European Organisation for Research and Treatment of Cancer (EORTC) aus; Hauptfragebogen (QLQ-C30) und Kopf-Hals-Tumor-Fragebogen (QLQ-HN35) jeweils vor definitiver oder adjuvanter IMRT (t0), am Ende der IMRT (t1), nach weiteren 6–8 Wochen (t2), 6 Monaten (t3) und nach 1 Jahr (t4).

Ergebnisse Insgesamt haben 111 Patienten zu allen fünf Zeitpunkten die Fragebögen ausgefüllt und wurden in die Studie eingeschlossen (Responserate t0: 99%; Ausfallrate t0–t4: 5%). Während der IMRT verschlechterten sich alle Domänen der LQ und besserten sich langsam über das erste Folgejahr. Viele Lebensqualitätswerte kehrten zum Ausgangsniveau zurück, während Probleme mit Riechen und Schmecken, trockener Mund und klebriger Speichel problematisch blieben. Probleme mit klebrigem Speichel wurden von Patienten nach definitiver IMRT häufiger berichtet als von Patienten nach adjuvanter Therapie ($F=3,5$; $P=0,05$).

Schlussfolgerung Nach einer IMRT dauert es bei Patienten mit Kopf-Hals-Tumoren bis zu 1 Jahr bis die LQ wieder ihr Ausgangsniveau erreicht; einige Domänen bleiben auch noch nach 1 Jahr darunter. Obwohl es Ziel der IMRT ist, Funktion und LQ zu erhalten, bleiben trockener Mund und klebriger Speichel teilweise als Langzeiteffekte bestehen, insbesondere bei Patienten nach primärer IMRT. Patienten sollten diesbezüglich vor Beginn der Therapie aufgeklärt werden, um ihnen Unzufriedenheit mit der Geschwindigkeit der Rekonvaleszenz zu ersparen.

Schlüsselwörter Rehabilitation · Xerostomie · Toxizität · Geschmackssinn · Geruchssinn

Patients with newly diagnosed head and neck cancer (HNC) face many issues that can impact on their quality of life (QoL). Treatment for locally advanced HNC (LAHNC) is usually multimodal, involving surgery, radiotherapy, and systemic therapy. Over recent years treatment has become

more intensive and is associated with a greater toxicity burden [1–3]. Side effects associated with treatment for HNC can have a profound effect on everyday activities. Surgery, if required, may leave patients with facial disfiguration depending on size and location of the tumor [4]. Finally, radiotherapy can affect structures adjacent to the tumor, which may result in xerostomia, dysphagia, trismus, and osteoradionecrosis [5, 6].

Assessing QoL is becoming increasingly important. Recent guidelines state that health-related QoL issues are of paramount importance: “Tumors affect basic physiological functions (i.e. the ability to chew, swallow, and breathe), senses (taste, smell, and hearing), and uniquely human characteristics (i.e. appearance and voice)” [2].

It has been shown that sparing both parotid glands during intensity-modulated radiation therapy (IMRT) reduces the incidence of xerostomia, dysphagia, and the number of patients requiring a percutaneous gastrostomy significantly [7]. IMRT was developed with the aim of reducing side effects of radiotherapy without compromising oncological efficacy [8]. Studies have shown that this aim has been achieved [9]; however, information is still lacking regarding the length of time needed by patients to completely recover some aspects of QoL. Healthcare practitioners armed with an understanding of which aspects of QoL are slow to recover may be better able to counsel patients as to what to expect in the future and provide additional support after treatment, potentially improving QoL. Likewise, a better understanding is needed of why some patients recover more easily than others; therefore, predictors of change in QoL should be explored in more detail.

The present study examined whether QoL in patients with LAHNC recovers to baseline levels within 1 year after IMRT. We also investigated which QoL areas improve and deteriorate during and after treatment, and what factors are related to these changes.

Patients and methods

Study design and sampling

Patients with LAHNC (nonmetastatic) who were treated with curative-intent IMRT (60–70 Gy at 2 Gy/fraction), either definitive or adjuvant, were eligible for this prospective study. Platinum-based chemotherapy (100 mg/m² on days 1, 22, and 43 or 30 mg/m² weekly) was administered [2, 10, 11]. Radiation dose was prescribed according to ICRU report 83. Sensitive structures were contoured and a margin of 2 mm applied. Depending on tumor site and nodal disease the dose constraints applied to the parotid glands and oral cavity/pharyngeal structures/larynx were ≤20 Gy and ≤30–36 Gy, respectively.

Eligible patients were approached consecutively by the radiation oncologist. Questionnaires were completed during scheduled visits. Approval was obtained from the local ethics committee. All patients provided written informed consent.

Endpoints

QoL was measured before IMRT (t0), at the end of IMRT (t1), 6–8 weeks (t2), 6 months (t3), and 1 year after IMRT (t4). Questionnaires were self-completed in the physician's office at these times. The German-language version of the European Organisation for Research and Treatment of Cancer (EORTC) 30-item Quality of Life Core Questionnaire (QLQ-C30) [12] and the 35-item Head and Neck module (HN35) [12] were used. The QLQ-C30 consists of a global health scale and five functioning scales (Emotional, Physical, Cognitive, Social, and Role), as well as three multi-item and six single-item symptom scales (Fatigue, Pain, Nausea and vomiting, Dyspnea, Insomnia, Appetite loss, Constipation, Diarrhea, and Financial difficulties). The HN35 includes seven head and neck-specific multi-item symptom scales (Pain in the mouth, Swallowing, Senses, Speech, Social eating, Social contact, and Sexuality), six single-item scales (Problems with teeth, Problems opening mouth, Dry mouth, Sticky saliva, Coughing, and Feeling ill) and five yes/no items (Use of painkillers, Nutritional supplements, Feeding tube, Weight loss, and Weight gain).

A score of 100 indicates perfect QoL on the functional scales, whereas for the symptom scales a score of 100 indicates a heavy burden. Score differences of 10 points or more between patient subgroups are considered to be clinically relevant [13]. The reliability and validity of the C30 and HN35 scales are considered acceptable [14, 15].

Toxicity (dysphagia, mucositis, and xerostomia) was rated at all assessment points between t0 and t4 using the Radiation Therapy Oncology Group (RTOG) toxicity criteria. Ratings were performed by the radiation oncologist (blinded to the QoL scores).

Weight and type of diet (parenteral, enteral, or oral) were documented.

Data analysis

Mean scores (\pm standard deviation) for the C30 and HN35 were calculated as defined in the EORTC manual [16], with a scale only being computed if the patient had completed at least half of its items. The distribution of the data was investigated visually. Changes over time were analyzed by calculating pairwise absolute differences between the measurement time points using matched-pair *t* tests.

An exploratory investigation of potential predictors of differences between baseline and 1 year after IMRT in key QoL domains (Senses, Dry mouth, and Sticky saliva) was performed using a multivariate generalized linear model analysis of variance with repeated measures. The selection of predictor variables to be tested was made *a priori* based on evidence from the literature and clinical experience. The same predictors were included in all models. Variables entered simultaneously were sequence of IMRT (definitive vs adjuvant treatment), tumor site (oral cavity vs other), and age (years).

Statistical analyses were performed using STATA version 10 (StataCorp, College Station, TX, USA).

Results

Patients

Patient enrollment began in March 2009 and the last patient included in this analysis was seen in March 2013. A total of 145 patients were included at baseline. One year after the baseline assessment, 115 patients (79%) were seen again; 28 patients (19%) had died, 1 patient (1%) was lost to follow-up, and 1 patient (1%) did not complete a QoL questionnaire. QoL measurements at all four time points were available for 111 patients (95% of those still alive 1 year after baseline). All of the analyses described herein are based on these 111 patients. Baseline characteristics of patients are shown in Table 1.

Treatment

Twenty-eight patients (25%) had received definitive chemoradiotherapy, 47 patients (42%) had adjuvant radiotherapy, 31 (28%) had adjuvant chemoradiotherapy, and 5 patients (5%) had radiotherapy only. In terms of parotid sparing, 39 patients (35%) received <26 Gy to both parotids, 62 (56%) received <26 Gy to one parotid, and 9 patients (8%) received >26 Gy to both parotids; this information was not available for 1 patient.

Changes in QoL over time

QoL deteriorated during IMRT, resulting in statistically significantly lower scores at the end of treatment compared with baseline on all C30 functioning scales, and higher scores for most symptom scales, indicating a greater degree of cancer-related symptoms (Table 2). A similar pattern was observed for the HN35, with statistically significantly higher scores at the end of treatment for all domains except Problems with teeth (Table 2; Fig. 1). Marked increases (>30 points) were observed at the end of IMRT compared

Table 1 Baseline characteristics ($n=111$)

Characteristic	Patients, n (%)
Sex, n (%)	
Male	78 (70)
Female	33 (30)
Age at baseline, years	
<50	19 (17)
50–59	35 (32)
60–69	43 (39)
≥ 70	14 (13)
Karnofsky performance score	
100	9 (8)
90	38 (34)
80	30 (27)
70	30 (27)
60	3 (3)
50	1 (1)
Tumor stage	
T1	22 (20)
T2	33 (30)
T3	25 (23)
T4	25 (23)
Tx	6 (5)
Nodal stage	
N0	24 (22)
N1	22 (20)
N2	60 (54)
N3	5 (5)
Treatment	
RT only	5 (5)
Definitive CRT	28 (25)
Adjuvant RT	47 (42)
Adjuvant CRT	31 (28)
Tumor site	
Oral cavity	35 (32)
Oropharynx	41 (37)
Hypopharynx/larynx	22 (20)
Nasopharynx	5 (5)
Nasal	4 (4)
Unknown primary	4 (4)

CRT chemoradiotherapy, RT radiotherapy.

with baseline in domains such as Swallowing (+37), Senses (+40), Social eating (+35), Dry mouth (+35), Sticky saliva (+51), and Feeding tube (+49), indicating clinically significantly poorer QoL at this time (Table 2).

One year after IMRT, all of the C30 functioning scores were equivalent to or higher than at baseline (Table 2). The largest improvements were observed in Social functioning (+12) and Global health status (+14). Most C30 symptom scores were lower 1 year after IMRT than at baseline, indicating better QoL; notably, Pain had decreased (–11). Most HN35 scores had recovered substantially (to baseline values or lower) by 1 year after IMRT (Table 2). However, some scores remained higher than at baseline, with clinically

meaningful increases still present in Senses (+14), Dry mouth (+28), and Sticky saliva (+15). A clinically and statistically significant improvement was seen for Felt ill (–18).

At the 1-year timepoint, a notable reduction was observed in the use of painkillers (–27 compared with baseline). A reduction in weight loss (–43) was observed, along with a corresponding increase in weight gain (Table 2).

Predictors of QoL changes

We also investigated predictors of QoL deterioration between baseline and 1 year (Table 3). Potential predictors tested were treatment (definitive radiotherapy or chemoradiotherapy vs adjuvant radiotherapy or chemoradiotherapy) and tumor site (oral cavity vs other sites), adjusted for age.

Mouth dryness deteriorated in all patients, regardless of age, treatment received, and site of the tumor. Sticky saliva issues increased to a greater extent in patients with definitive versus adjuvant IMRT ($F=3.5$; $P=0.05$). Patients who had definitive IMRT had fewer problems with Sticky saliva before IMRT than those who had surgery before IMRT. However, 1 year after the start of therapy, patients with definitive IMRT had greater problems with Sticky saliva than those who had received adjuvant IMRT. Problems with Sticky saliva increased over time in both groups. Increases in problems with Senses, which was a significant factor in the univariate analysis (data not shown), were not confirmed in the multivariate analysis.

Nutrition

The patients' average body mass index (BMI) decreased from 25.1 kg/m² at baseline to 23.5 kg/m² at the end of IMRT, and further decreased to 22.8 kg/m² at 3 and 6 months after IMRT. By 1 year post-IMRT, mean BMI had increased to 23.3 kg/m².

The proportion of patients with a percutaneous endoscopic gastrostomy (PEG) tube increased from 42% at baseline to 75% at the end of treatment. From 6 weeks after IMRT onwards, the proportion of patients with a PEG tube decreased slowly but steadily from 68% after 6–8 weeks, to 42% after 6 months, and 31% after 1 year.

Parenteral nutrition was rarely needed. Before treatment, one patient (0.9%) used parenteral nutrition; this increased to 7% ($n=8$) at the end of IMRT, then decreased to 4% ($n=5$) at 6–8 weeks after IMRT, 3% ($n=3$) at 6 months after IMRT, and 0.9% ($n=1$) by 1 year after IMRT.

Toxicity

Dysphagia, as assessed by the radiation oncologist, was common at the end of IMRT; over 40% of patients had

Table 2 Evolution of general QoL, measured using the EORTC QLQ-C30 and HN35 during and after treatment. Values in bold are changes of ≥ 10 points. Positive changes imply improved function or more symptoms over time. Negative changes imply worsened function or fewer symptoms over time

Mean (SD) scale score ^a	Timepoint					Δ t0–t1 ^b	P_{t0-t1} ^c	Δ t0–t4 ^b	P_{t0-t4} ^c
	t0	t1	t2	t3	t4				
QLQ-C30									
<i>Functioning scales</i>									
Physical functioning	77 (23)	60 (24)	72 (21)	77 (22)	78 (23)	-17	<0.01	1	0.73
Role functioning	58 (37)	36 (33)	55 (30)	63 (30)	68 (30)	-21	<0.01	11	0.02
Emotional functioning	59 (29)	46 (25)	60 (26)	67 (25)	67 (24)	-13	<0.01	7	0.02
Cognitive functioning	79 (26)	67 (26)	79 (22)	78 (22)	79 (22)	-12	<0.01	0	0.86
Social functioning	60 (34)	38 (30)	56 (29)	63 (30)	72 (27)	-22	<0.01	12	<0.01
Global health status	50 (24)	35 (23)	54 (21)	59 (21)	64 (21)	-15	<0.01	14	<0.01
<i>Symptom scales</i>									
Fatigue	41 (29)	67 (26)	48 (26)	39 (25)	38 (26)	26	<0.01	-2	0.46
Nausea and vomiting	7 (15)	35 (33)	16 (24)	6 (12)	4 (10)	29	<0.01	-3	0.11
Pain	38 (34)	57 (34)	32 (30)	26 (28)	27 (29)	19	<0.01	-11	<0.01
Dyspnea	25 (30)	33 (31)	26 (31)	22 (29)	23 (29)	8	0.01	-2	0.55
Insomnia	38 (34)	54 (35)	37 (34)	36 (34)	34 (33)	15	<0.01	-4	0.32
Appetite loss	27 (36)	69 (36)	39 (37)	27 (34)	24 (33)	41	<0.01	-2	0.60
Constipation	11 (24)	33 (36)	20 (29)	13 (26)	12 (24)	22	<0.01	1	0.83
Diarrhea	13 (25)	21 (32)	13 (24)	8 (19)	10 (23)	8	0.03	-4	0.21
Financial difficulties	32 (36)	39 (35)	35 (35)	32 (34)	31 (35)	8	0.02	-1	0.75
HN35									
<i>Multi-item symptoms scales</i>									
Pain in the mouth	29 (26)	58 (29)	31 (23)	23 (23)	20 (23)	29	<0.01	-9	<0.01
Swallowing	33 (32)	70 (24)	41 (30)	35 (30)	29 (29)	37	<0.01	-4	0.22
Senses	21 (28)	61 (27)	45 (30)	40 (30)	35 (29)	40	<0.01	14	<0.01
Speech	33 (30)	61 (30)	36 (28)	32 (28)	28 (26)	28	<0.01	-5	0.11
Social eating	33 (31)	68 (29)	47 (33)	40 (34)	33 (30)	35	<0.01	0	0.93
Social contact	17 (20)	35 (28)	20 (21)	18 (22)	14 (18)	17	<0.01	-3	0.15
Sexuality	45 (39)	70 (37)	50 (38)	51 (38)	40 (38)	22	<0.01	-7	0.16
<i>Single-item symptom scales</i>									
Problems with teeth	25 (35)	28 (35)	23 (33)	23 (31)	31 (37)	5	0.29	3	0.40
Problems opening mouth	33 (38)	63 (39)	41 (37)	37 (37)	35 (36)	29	<0.01	3	0.51
Dry mouth	33 (33)	68 (35)	69 (34)	68 (30)	60 (30)	35	<0.01	28	<0.01
Sticky saliva	35 (36)	86 (26)	64 (35)	53 (35)	50 (35)	51	<0.01	15	<0.01
Coughed	38 (32)	65 (32)	39 (31)	40 (32)	39 (28)	28	<0.01	2	0.69
Felt ill	43 (33)	68 (31)	38 (30)	29 (28)	25 (26)	26	<0.01	-18	<0.01
<i>Additional items</i>									
Painkillers	51 (50)	74 (44)	49 (50)	34 (48)	24 (43)	23	<0.01	-27	<0.01
Nutritional supplements	18 (39)	46 (50)	44 (50)	31 (46)	25 (44)	29	<0.01	7	0.21
Feeding tube	25 (43)	73 (45)	60 (49)	41 (49)	29 (46)	49	<0.01	4	0.44
Weight loss	59 (49)	77 (42)	50 (50)	30 (46)	16 (37)	18	<0.01	-43	<0.01
Weight gain	15 (36)	5 (21)	24 (43)	35 (48)	43 (50)	-10	0.02	29	<0.01

D change, *EORTC* European Organisation for Research and Treatment of Cancer, *HN35* Head and Neck module, *IMRT* intensity-modulated radiation therapy, *QLQ-C30* Quality of Life Questionnaire Core module, *QoL* quality of life, *SD* standard deviation, *t* timepoint

^aUnadjusted means (SDs) of QoL before and after IMRT

^bMean change over time (mean of individual differences between two assessment points)

^c*P* value for matched signed-rank tests comparing QoL at baseline (t0) with QoL after IMRT (t1 and t4).

grade 3 dysphagia at this time, and although this decreased over time, 11 % of patients still had grade 3 symptoms after

1 year (Fig. 2). Physician-assessed xerostomia also peaked at the end of IMRT and declined thereafter, with 14 % of patients having grade 2 xerostomia 1 year after IMRT.

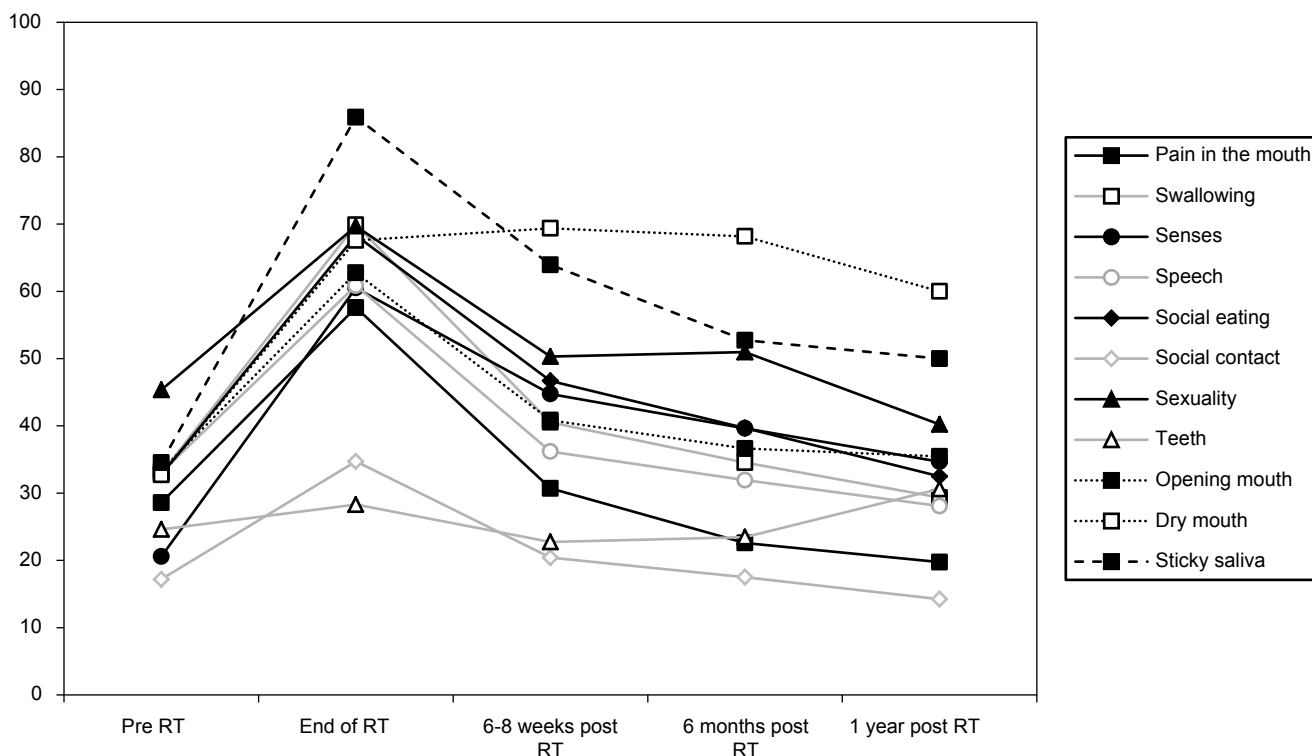


Fig. 1 Changes in European Organisation for Research and Treatment of Cancer quality of life questionnaire Head and Neck Module scores over time before IMRT (t0), at the end of IMRT (t1), 6–8 weeks after

IMRT (t2), 6 months after IMRT (t3), and 1 year after baseline (t4) in patients with head and neck cancer (n=111). Unadjusted mean scores. (IMRT intensity modulated radiotherapy, RT radiotherapy, t timepoint)

Table 3 Predictors of quality of life deterioration in patients with head and neck cancer before and 1 year after intensity-modulated radiotherapy (IMRT). Values in bold are those with evidence of an effect modification of time by a predictor

Domain	Time		Time * oral cavity (vs other sites)		Time * adjuvant IMRT (vs definitive IMRT)		Time * age	
	F ^a	P	F ^a	P	F ^a	P	F ^a	P
Senses	0.1	0.83	0.9	0.36	0.1	0.80	0.2	0.67
Dry mouth	4.9	0.03	1.7	0.20	0.1	0.83	1.2	0.28
Sticky saliva	0.2	0.69	0.7	0.40	3.5	0.05	0.1	0.77

^aF-statistics of multivariate generalized linear model analysis of variance with repeated measures.

Grade 2/3 mucositis was also common at the end of treatment but was negligible by the 1-year time point.

Discussion

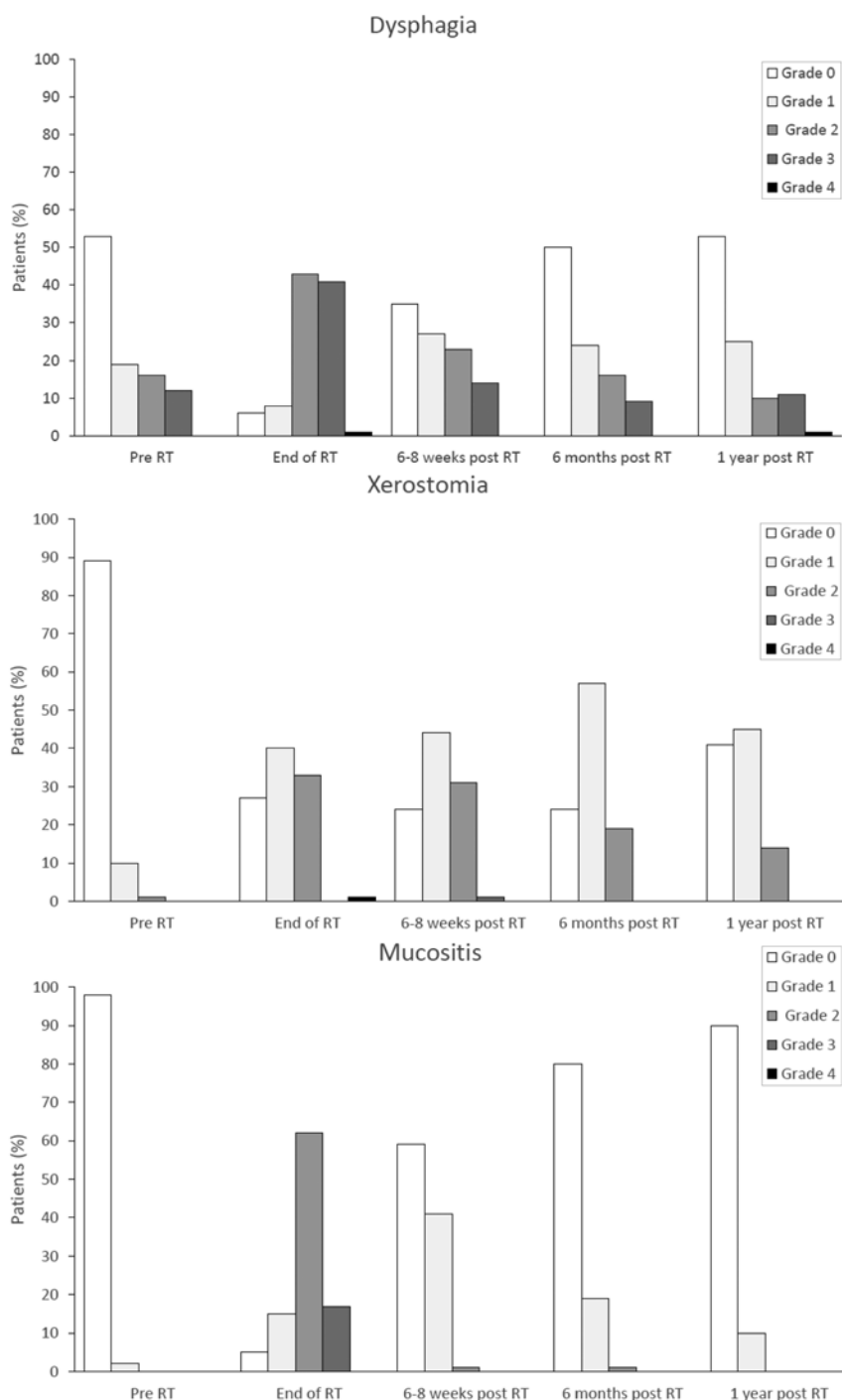
This longitudinal analysis of patients undergoing IMRT for the treatment of HNC has demonstrated that patients experience significant deterioration of their QoL during IMRT. Some important QoL areas improve considerably by 1 year after treatment, although others remain compromised. This is in line with previous reports that rehabilitation after multimodal treatment for HNC can take a year or more [9].

Pain, Social functioning, and Global health status improved to a clinically meaningful extent when assessed 1 year after the end of treatment compared with baseline,

indicating that patients were generally feeling better and more at ease in social situations than they had been before the start of treatment. Similar patterns of recovery of Global Health Status after treatment have been reported in some studies [17–19]; others, in contrast, observed no change compared with baseline in Global Health Status at 1 year [20], suggesting that this measure is dependent on a number of factors, including baseline scores and complexity of treatment.

In contrast, the scores for the HNC-specific domains Senses (problems with sense of taste or smell), Dry mouth, and Sticky saliva were all still clinically meaningfully worse than their baseline levels 1 year after IMRT, although scores had recovered from the peaks observed at the end of IMRT. Similar results have been reported from other studies [17, 19, 20], clearly demonstrating that recovery from

Fig. 2 Incidence of selected adverse events before, during, and after intensity-modulated radiotherapy in patients with head and neck cancer. Adverse events assessed by the radiation oncologist using Radiation Therapy Oncology Group toxicity criteria. (RT radiotherapy)



dry mouth is slower than other adverse effects of treatment. In their systematic review of 37 QoL studies in patients with HNC, So et al. [21] reported that problems with Dry mouth, Sticky saliva, and Fatigue were most often compromised 1 year after therapy. Indeed, several longer-term QoL studies of patients undergoing treatment for HNC showed that Senses, Dry mouth, and Sticky saliva scores had not returned to baseline 5 years after treatment [18, 22, 23]. Oskam et al. [24] did not observe a return to baseline values

in their long-term (96–131 months) assessment of patients with oral and oropharyngeal cancers, which suggests that these aspects may never return to pretreatment levels. Further assessment of our patients beyond 1 year will provide additional information.

Physical problems were apparently ongoing in the present study after 1 year, as demonstrated by the incidences of oncologist-assessed RTOG xerostomia and dysphagia and the patient-reported Dry mouth and Sticky saliva scores

observed at the end of the study. One might thus expect that Global Health Status scores would remain compromised throughout the observation period, particularly as both xerostomia [25] and dysphagia [26, 27] have been shown to correlate with QoL in previous studies. The fact that this was not the case suggests that the effect of xerostomia on global QoL is relatively limited in the absence of acute mucositis [28]. Another possible explanation is that patients mentally adjust to their disease, resulting in a better overall judgment of their life in general, even when some QoL aspects are still impaired. For example, Morton [29] reported adaptation to dysfunction in a retrospective analysis of QoL in patients with HNC, as demonstrated by scores for perceived difficulty in swallowing, which decreased despite an ongoing need for a soft or liquid diet.

Clinically meaningful improvements compared with baseline were recorded at 1 year in objective HNC-specific considerations including feeling ill, using painkillers, and gaining weight. Mean BMI values fell during IMRT, but had started to recover in the 6–12 months posttreatment. These findings support the suggestion that patients genuinely feel better after the immediate effects of therapy have abated and that xerostomia-related issues do not detract from their general well-being in the longer term. Pow et al. [17] also reported an increased proportion of patients with weight gain 1 year after IMRT, but no overall reduction in the use of painkillers.

After 1 year, the incidence of sticky saliva and dry mouth in our study was greater among patients treated with definitive chemoradiotherapy than in those who had adjuvant chemoradiotherapy, despite the opposite having been the case before treatment. This may be related to the fact that in the absence of tumor less volume was irradiated to a higher dose or because parotid sparing was more likely to be a feasible option. Alternatively, it may be related to the small size of the definitive chemoradiotherapy group compared with the adjuvant group. Further studies are required to establish whether this is a true effect or a chance finding.

The relationship between QoL and xerostomia underlines the importance of minimizing side effects during treatment by sparing the salivary glands where possible. A focus of treatment planning has been to spare the parotid and submandibular glands and oral cavity, which was shown to significantly reduce the incidence of both xerostomia and dysphagia [7, 30, 31]. Xerostomia continues to be a problem. Better strategies for its prevention and treatment are clearly needed. Measures investigated to date have included submandibular gland transfer [32], amifostine [33], pilocarpine [34], and acupuncture [35, 37]. To date, there is no strong evidence that these interventions significantly improve saliva flow or dry mouth symptoms [37, 38].

One of the strengths of this study was that few patients were lost to follow-up, strengthening the conclusions drawn

from the data. Observational studies, while less rigorously controlled than randomized clinical trials, have the advantage of more accurately reflecting the real-life clinical situation because they suffer less frequently from selection bias that can result from excluding patients based on factors such as comorbidity and age.

Conclusion

This analysis has demonstrated that LAHNC patients treated with IMRT and their health care providers can expect that most aspects of QoL will substantially recover within a year of treatment. Xerostomia-related issues appear to persist at this time point but do not impact on overall QoL. Patients should be counseled at the start of therapy to reduce disappointment in the pace of recovery with its potentially negative impact on QoL.

Compliance with ethical guidelines

Conflict of interest S. Tribius, M. Raguse, C. Voigt, A. Münscher, A. Gröbe, C. Petersen, A. Krüll, C. Bergell and S. Singer state that there are no conflicts of interest.

All studies on humans described in the present manuscript were carried out with the approval of the responsible ethics committee and in accordance with national law and the Helsinki Declaration of 1975 (in its current, revised form). Informed consent was obtained from all patients included in studies

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