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Original article

A prospective evaluation of patient-reported quality-of-life after (chemo)radiation for oropharyngeal cancer: Which patients are at risk of significant quality-of-life deterioration?

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ABSTRACT

Background and purpose: To prospectively investigate the impact of different patients' characteristics on quality-of-life (QoL) after (chemo)radiation for oropharyngeal cancer (OPC).
Materials and methods: Between 2008 and 2011, 207 patients were treated with 46-Gy of (chemo)-IMRT followed by a boost by means of IMRT, brachytherapy (BT), or Cyberknife (CK). QoL-assessment was performed using the EORTC QLQ-C30, and QLQ-H&N35-questionnaires at baseline, end of treatment, 2, 4, 6 weeks and 3, 6, 12, and 18 months after treatment. The correlation between patients' characteristics (AJCC-stage, tumor subsite, chemotherapy, neck dissection, unilateral neck irradiation, and boost technique), and changes in QoL over time were investigated.
Results: At 18 months, improvements were seen in QLQ-C30 emotional functioning, insomnia, and pain and QLQ-H&N35 pain and speech. The scores on QLQ-H&N35 swallowing returned to baseline level while the scores on dry mouth, sticky saliva, opening mouth, and teeth were significantly deteriorated compared to baseline. Boost techniques and unilateral neck irradiation were significantly predictive for dry mouth, swallowing and opening mouth while chemotherapy was correlated with changes on swallowing and opening mouth scales.
Conclusions: The most significant deterioration was seen in patient-related xerostomia. Boost technique, unilateral neck irradiation and chemotherapy were significantly predictive for QoL-changes over time.
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Over the last few decades, loco-regional control and survival in patients with head-and-neck cancer (HNC) were improved as a result of implementing several new strategies such as concomitant chemoradiotherapy, altered fractionation schemes of radiotherapy, the use of induction chemotherapy and the integration of EGFR-inhibitors [1]. However, these improvements were achieved at the cost of important toxic effects. As a consequence of survival improvement achieved, the impact of disease and treatment on patient's overall well-being and functioning has become an important secondary consideration and a topic of growing interest in clinical research and practice. Therefore, our department has decided to prospectively evaluate the impact of different patients' characteristics on patients' quality-of-life (QoL). From 2008, prospective QoL-assessment was performed in all patients with HNC treated in our institution, including baseline assessment.

The purpose of the current study is to report on outcomes of a prospective evaluation of patient-reported QoL after (chemo)radiotherapy for oropharyngeal cancer (OPC) and to identify subgroups of patients at risk of significant changes of QoL-scores after treatment.

Materials and methods

Between January 2008 and June 2011, 239 consecutive patients with OPC, treated with curative intention by (chemo)radiotherapy at the department of Radiation Oncology of our institution. However, only patients who were NED and filled out the questionnaires at baseline & at least on 3 moments during the follow-up are considered as responders and included in the analysis (n = 207.87%).

QoL-assessment was obtained at baseline, at the end of treatment, at 2, 4, 6 weeks and at 3, 6, 12, and 18 months after treatment. The questionnaires were handed over to patients by the nurse of our department. Patients were instructed to answer the questions at the specific points in time and return the questionnaires to the department. Two types of questionnaires were used:

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the European Organisation for Research and Treatment of Cancer Quality-of Life-Questionnaire-C30 (EORTC QLQ-C30) and the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire-Head and Neck 35 (EORTC QLQ-H&N35) [2]. The questionnaires have been translated into Dutch.

The EORTC QLQ-C30 is a cancer-specific questionnaire and incorporates a global QoL-score, five functional scales, three symptom scales, and six single items. Higher scores for the global QoL scale and for a functional scale indicate a better level of functioning, whereas higher scores for a symptom scale or a single-item scale denote more severe symptoms and worse QoL.

The EORTC-H&N35 is a site-specific questionnaire designed to assess QoL in HNC patients and incorporates seven multiple-item and six single-item scales to assess different commonly-reported symptoms after treatment of HNC. The higher the score, the more problems the patient will have.

Only QoL changes over time of $\geqslant$10 points were considered clinically relevant. Osaba et al. [3] determined the significance of the numerical changes in time and suggested that "moderate changes" (mean change 10–20) to be clinically relevant.

The treatment protocol of OPC at our institution consists of an initial series of 46-Gy of IMRT (23 fractions, 2 Gy/fraction, 6 fractions/week) to the primary tumor and the neck, either unilaterally in well-lateralized OPC (tumors confined to tonsillar fossa, soft palate with at least 1 cm from the midline or lateral pharyngeal wall) or bilaterally in other cases. In case of T1–2 and small T3 tumors, a boost by means of brachytherapy (BT) was given to the primary tumor (22-Gy) and in case of node-positive disease, neck dissection (ND) was performed at the same session of the brachytherapy. Patients who were not suitable for the standard brachytherapy boost were offered a boost by means of the Cyberknife (CK) (Robotic Stereotactic Radiosurgery System). In patients with T4 and large T3 tumors, a boost of 24-Gy by means of IMRT (12 fractions, 2-Gy/fraction, 6 fractions/week) was given to the primary tumor alone in case of N0 and to the primary tumor and the involved neck in case of node-positive disease [4]. When chemotherapy was indicated (T3, T4 or N3), two cycles of cisplatin were given (100 mg/m^2 on day 1 and 22 of radiotherapy).

Table 1
Patient's characteristics & treatment data (n = 207).

	No. of patients (%)
Gender	
Male	143 (69)
Female	64 (31)
Age	
<65 years	142 (69)
$\geqslant$65 years	65 (31)
Follow-up (months)	
Median	27
Range	13–40
AJCC tumor stage	
I	5
II	28
III	21
IV	6
Tumor stage	
T1	18
T2	48
T3	20
T4	14
Nodal stage	
N0	38
N1	18
N2	41
N3	3
Tumor subsite	
TF/SP	65
Others	35
UNI	
Yes	38
No	62
Chemotherapy	
Yes	30
No	70
Neck dissection	
Yes	37
No	63
Boost technique	
IMRT	36
BT	35
CK	29

Abbreviations: AJCC, American Joint Committee on Cancer; TF, tonsillar fossa; SP, soft palate; BOT, base of tongue; UNI, unilateral nodal irradiation; IMRT, intensity-modulated radiotherapy; BT, brachytherapy; CK, cyberknife.

Statistical analysis

Scores of all scales were transformed onto a 0–100 scale. Mean scores for the QLQ-C30 and QLQ-H&N35 were calculated according to the EORTC scoring manual. Missing data in QoL items were imputed according to the EORTC scoring manual [5]. The impact of different patients' characteristics (AJCC-stage, tumor subsite, chemotherapy, ND, unilateral neck irradiation, and boost technique) on QoL was analyzed using Kruskal–Wallis rank test. All significant tests were two-sided and p values <0.05 were considered statistically significant.

Results

Table 1 summarizes patients' characteristics.

Quality of life at baseline

The QLQ-C30 scores of the whole group at baseline were worse than the reference German and West European population [6]. The greatest symptom burden was for role and emotional functioning, fatigue, pain, insomnia, and appetite loss. All patients had also substantial head and neck symptoms at baseline as measured with the highest scores for pain, swallowing, dry mouth, and sexuality (Table 2).

Quality of life changes over time

Overall QoL-scores on all scales deteriorated during treatment, reaching the worst scores around the end of treatment. For the EORTC QLQ-C30, the scores on all scales started to improve within 2–4 weeks and returned to almost baseline levels at 6–12 months after treatment. At 18 months, clinically relevant and statistically significant improvements were seen in emotional functioning and insomnia. The pain experience had also significantly improved (Table 2). None of tested variables correlated significantly with these improvements.

The scores on almost all scales of the EORTC QLQ-H&N35 took longer to improve toward baseline levels. At 18-months, the scores on the QLQ-H&N35 pain and speech had significantly improved, compared to baseline. The scores on the QLQ-H&N35 swallowing returned to baseline level while scores on teeth and opening mouth scales were significantly deteriorated compared to baseline, although the changes were clinically not relevant ($\leqslant$10 points). Clinically relevant and statistically significant deterioration were found on dry mouth and sticky saliva scales (Table 2).

Correlation QoL changes over time and patients' demographics

Six clinical predictive factors for changes in QoL over time were tested using Kruskal–Wallis rank test. AJCC-stage, tumor

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Table 2
Mean values and *p*-values for all scales of the EORTC QLQ-C30 and the EORTC QLQ-H&N35.

	Scores at baseline	Scores at EOT	Scores at 6 months	Scores at 12 months	Scores at 18 months	Δ0–18 m	*p*-Value
Global QoL scale (100 = favorable)	72.1	48.1	71.1	74.0	71.7	−0.5	0.768
Functional scales (100 = favorable)							
Physical functioning	87.1	66.6	81.9	83.4	84.1	−3.0	0.414
Role functioning	81.8	52.9	75.8	82.0	81.7	−0.1	0.624
Emotional functioning	71.0	67.3	80.4	80.8	81.3	**+10.3**	**<0.001**
Cognitive functioning	87.8	76.0	85.3	86.4	83.6	−4.2	0.467
Social functioning	87.3	69.4	86.7	88.5	87.0	−0.3	0.446
Symptom scales (100 = unfavorable)							
Fatigue	22.4	55.6	28.8	25.0	25.1	−2.7	0.493
Nausea and vomiting	3.2	29.5	4.9	4.9	6.8	−3.6	0.131
Pain	21.6	49.8	19.6	14.1	14.8	+6.8	**0.018**
Single items (100 = unfavorable)							
Dyspnea	10.8	15.6	12.4	12.5	15.1	+4.3	0.484
Insomnia	25.6	30.7	14.8	15.4	14.9	**+10.7**	**0.002**
Appetite loss	13.0	58.3	20.2	17.3	15.5	−2.5	0.398
Constipation	7.1	25.3	9.1	7.3	10.5	−3.4	0.505
Diarrhea	5.1	13.6	7.1	5.8	5.5	−0.4	0.970
Financial difficulties	10.7	14.4	14.3	15.0	14.6	−3.9	0.168
Multiple-item scales (100 = unfavorable)							
Swallowing	21.4	64.6	27.0	23.6	21.9	−0.5	0.840
Pain	31.1	60.0	29.2	23.3	24.2	+6.9	**0.018**
Senses	11.2	54.3	23.0	19.6	16.3	−5.1	0.331
Speech	13.5	40.7	14.2	10.7	9.7	+3.8	**0.037**
Sexuality	21.8	52.4	26.6	22.2	24.6	−2.8	0.407
Social eating	13.9	53.0	24.6	20.9	16.6	−2.7	0.080
Social contact	4.7	19.7	5.1	5.0	5.7	−1	0.936
Single-item scales (100 = unfavorable)							
Dry mouth	21.8	65.3	57.2	52.2	48.4	**−26.6**	**<0.001**
Sticky saliva	16.7	77.5	45.0	36.5	41.8	**−25.1**	**<0.001**
Teeth	15.6	28.3	19.5	17.5	22.4	−6.8	**0.037**
Opening mouth	16.1	47.4	25.6	23.5	24.6	−8.5	**0.012**
Cough	19.4	40.6	24.1	22.6	23.3	−3.9	0.643
Feeling ill	12.4	47.2	12.4	12.2	13.2	−0.8	0.777

Abbreviations: EORTC QOL-C30, The European Organisation for Research and Treatment of Cancer Quality-of Life-Questionnaire-C30; EORTC QOL-H&N35, The EOTRC Quality-of Life-Questionnaire Head and Neck 35; EOT, end of the treatment; Δ0–18 m, changes in quality of life (mean scores) over time. Δ ⩾ 10 = clinically relevant, according to Osaba et al. [3]; + means improved function or reduced level of symptoms over time; − means deteriorated function or increased level of symptoms over time. Significant *p*-values ($p \leqslant 0.05$) and clinically relevant changes over time (⩾10) are indicated in bold.

subsite, and ND did not show significant correlation with QoL changes over time on any scale. Boost technique and unilateral neck irradiation (UNI) were significantly predictive for changes over time on QLQ-H&N35 dry mouth, swallowing and opening mouth scales. Patients received an IMRT-boost had statistically significant and clinically relevant deterioration over time, compared to CK and BT. At 18 months, the scores on dry mouth scale for patients treated by means of IMRT-boost, compared to CK and BT were 61 vs. 42, respectively ($p = 0.022$), on swallowing scale were 33 vs.17, respectively ($p = 0.038$) and on opening mouth scale were 40 vs. 21, respectively (0.032) (Figs. 1–3). When the scores on these scales were analyzed separately for BT and CK, the differences between the two boost techniques were neither statistically significant nor clinically relevant. The mean scores for BT and CK were 40 and 46 for dry mouth, 15 and 20 for swallowing, and 18 and 23 for opening mouth scales, respectively ($p > 0.05$) (Fig. 4).

With regard to the neck irradiation, the scores at 18 months on dry mouth scale for patients treated with UNI vs. bilateral neck irradiation were 38 vs. 54, respectively ($p = 0.026$), on swallowing scale were 14 and 19, respectively (0.046), and on opening mouth scale were 16 and 28, respectively ($p = 0.032$) (Figs. 1–3).

Chemotherapy was significantly predictive for changes over time on swallowing and opening mouth scales. At 18 months the scores on swallowing scale were 30 and 18, respectively for patients treated by chemoradiation and radiotherapy alone ($p = 0.042$) and on opening mouth scale were 40 and 20, respectively ($p = 0.030$) (Figs. 2 and 3).

Discussion

To the best of our knowledge, the present study represents the largest series to date where prospective QoL-assessment was done including baseline scores for patients with OPC treated by (chemo)radiation with highly-conformal radiation techniques.

QoL-scores on all scales deteriorated during treatment, reaching the worst scores around end of treatment and started to improve within 4–12 weeks later. At 18 months, the scores on the EORTC QLQ-C30 were returned to almost baseline levels, while statistically significant and clinically relevant deteriorations were still reported on QLQ-H&N35 dry mouth and sticky saliva scales. From the tested variables, AJCC stage, tumor subsite, and ND showed no statistically significant correlation with changes over time on any scale of the QLQ-H&N35. Boost techniques and UNI correlated significantly with changes over time on dry mouth, swallowing and opening mouth while chemotherapy with changes on swallowing and opening mouth scales.

According to Vergeer et al. [7], patient-related xerostomia was significantly reduced by using IMRT, compared to 3DCRT. However, these scores were still high; 48. Our study showed also that, despite the highly-conformal techniques used, xerostomia remains a major problem.

In the current study, the severity of xerostomia was significantly reduced in patients treated by means of BT or CK, compared to IMRT-boost and in those who received UNI, compared to bilateral neck irradiation. The dose conformality afforded by the use of BT and CK and the reduced margins used in these techniques (no CTV-PTV margin in case of BT and 3 mm margin in case of

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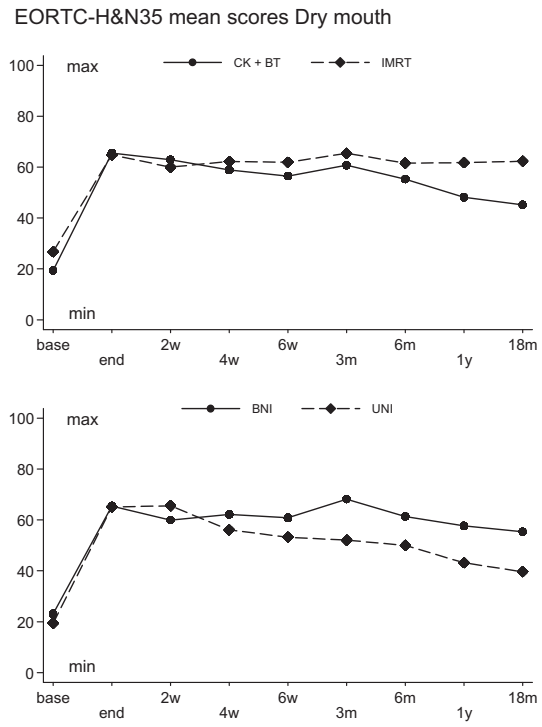

Fig. 1. The mean scores of the EORTC QLQ-H&N35 dry mouth scale for the most significant predictive factors: boost technique (CK, cyberknife; BT, brachytherapy; IMRT, intensity-modulated radiotherapy) and neck irradiation (UNI, unilateral neck irradiation; BNI, bilateral neck irradiation).

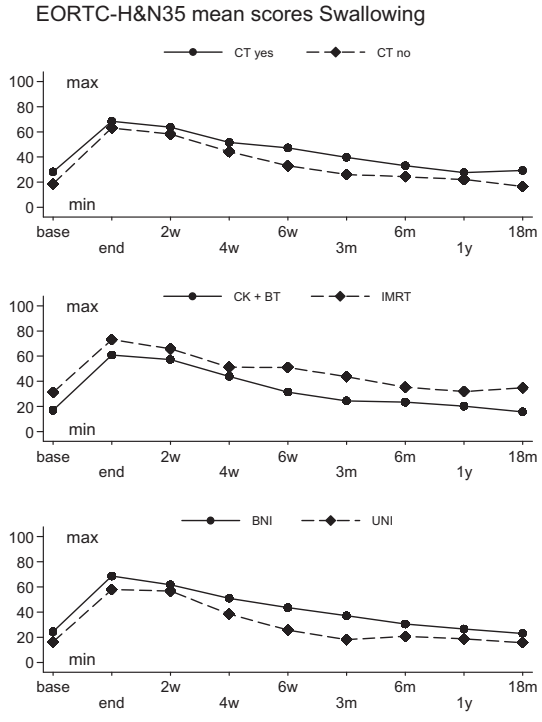

Fig. 2. The mean scores of the EORTC QLQ-H&N35 swallowing scale for the most significant predictive factors: chemotherapy (CT), boost technique (CK, cyberknife; BT, brachytherapy; IMRT, intensity-modulated radiotherapy), and neck irradiation (UNI, unilateral neck irradiation; BNI, bilateral neck irradiation).

CK, compared to 5 mm margin for IMRT-boost) seem to have a substantial effect on the dose received by the adjacent organs at risk, especially salivary glands and swallowing muscles, and

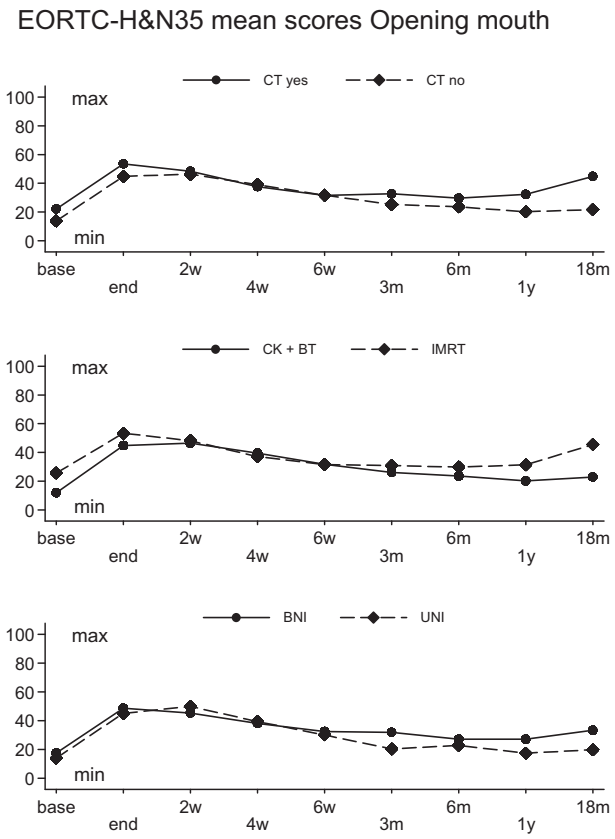

Fig. 3. The mean scores of the EORTC QLQ-H&N35 opening mouth scale for the most significant predictive factors: chemotherapy (CT), boost technique (CK, cyberknife; BT, brachytherapy; IMRT, intensity-modulated radiotherapy), and neck irradiation (UNI, unilateral neck irradiation; BNI, bilateral neck irradiation).

subsequently yielded a significant reduction in patient-reported xerostomia and dysphagia.

The impact of UNI on outcomes and toxicity was recently evaluated in 185 patients with well-lateralized OPC treated at our institution. Only 6 regional failures (RF) were reported (3.2%); 2 were contralateral (1.1%). The incidence of grade $\geqslant 2$ late toxicity xerostomia and dysphagia was 7% and 5.4%, respectively [4]. The main concern when excluding the contralateral neck from radiation treatment is the possibly increased risk of contralateral RF. However, in several studies [4,8], the incidence of contralateral RF was far below 5%. In the current study, UNI was significantly predictive for changes over time on QLQ-H&N35 dry mouth, swallowing, and opening mouth scales. The data from these studies suggest that a less conservative approach with regard to the selection of patients for UNI may well be justified in order to reduce the incidence of late toxicity but this needs further investigations in prospective trials.

Despite the substantial gains realized in the last decades further reduction of radiation-induced toxicity and improvement of QoL are still needed, given the increasing incidence of HPV-related OPC, especially among younger patients [9]. Besides parotid- and submandibular gland-paring, further reduction of the incidence and severity of xerostomia might be achieved by reducing the dose to the oral cavity. According to Little et al. [10], both observer- and patient-reported xerostomia were significantly lowered when the mean dose in oral cavity was kept below 50-Gy. Further reduction of dysphagia could probably be achieved by limiting the dose to constrictor pharyngeal muscles. Levendag et al. [11] reported a steep dose–effect relationship, with an increase of the probability of dysphagia of 19% with every additional 10-Gy to superior and

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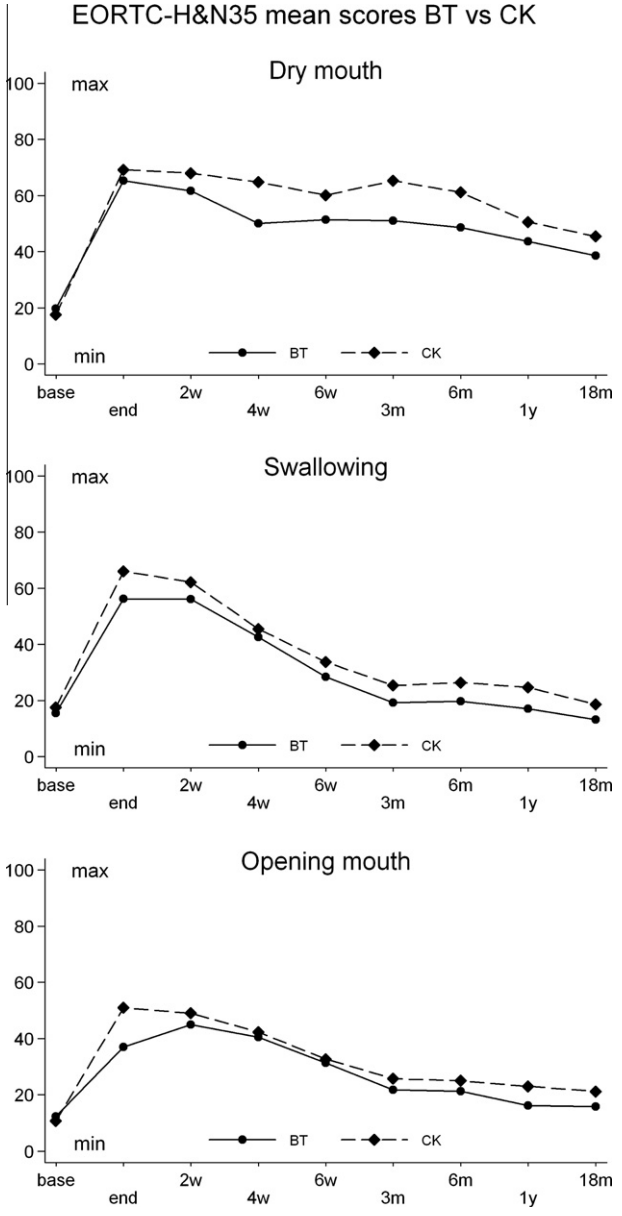

Fig. 4. The mean scores of the EORTC QLQ-H&N35 by boost technique: cyberknife (CK) vs. brachytherapy (BT) for dry mouth, swallowing, and opening mouth scales.

middle constrictor muscles. Trismus is another radiation-induced complication with a significant negative impact on QoL. Teguh et al. [12] found a significant correlation between dose in pterygoid muscles and trismus ($p = 0.02$). In that study, a steep dose–effect relationship was observed between mean dose and the probability of having trismus. For every 10-Gy in the pterygoid muscle, after a dose of 40-Gy, an increase of probability of trismus of 24% was observed. Since limiting the dose to the mastication apparatus is often not an aim in the current dose planning, more attention should be paid in the future to reduce the dose to these structures during treatment optimization.

Recently, there is accumulating evidence that (robotic) surgery for OPC might result in similar outcome and QoL-scores to (chemo)radiotherapy with slightly more swallowing problems and less xerostomia for patients treated surgically [13]. However, comparison with these studies is hampered by the major differences in patient's characteristics, the differences in the instruments used for QoL-assessment and the adjuvant therapy applied, the short follow-up and the small number of patients treated in these studies.

Conclusions

The current study presents the results of prospective QoL-assessment after (chemo)radiation for OPC using the EORTC QLQ-C30, and QLQ-H&N35-questionnaires. Statistically significant and clinically relevant deterioration was seen on QLQ-H&N35 dry mouth and sticky saliva. From the tested variables, AJCC-stage, ND and tumor subsites did not correlate with QoL changes over time on any scale. Boost technique, unilateral neck irradiation and chemotherapy were significantly predictive for QoL-changes over time, mainly on dry mouth, swallowing and opening mouth scales. Patient-related xerostomia was significantly lowered in patients treated by means of BT or CK, compared to IMRT-boost and patients in whom UNI was applied. Expanding the indications for these modalities needs to be thoroughly investigated in prospective trials.

Conflicts of Interest

None.

References

[1] Haddad RI, Shin DM. Recent advances in head and neck cancer. N Eng J Med 2008;359:1143–54.
[2] Bjordal K, de Graeff A, Fayers PM, Hammerlid E, van Pottelsberghe C, Curran D, et al. A 12 country field study of the EORTC QLQ-C30 (version 3.0) and the head and neck cancer specific module (EORTC QLQ-H&N35) in head and neck patients. EORTC Quality of Life Group. Eur J Cancer 2000;36:1796–807.
[3] Osaba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 1998;16:139–44.
[4] Al-Mamgani A, van Rooij P, Fransen D, Levendag PC. Unilateral neck irradiation for well-lateralized oropharyngeal cancer 2012 (in Press).
[5] Fayers PM, Aaronson NK, Bjordal K, Curran D, Groenvold M, On behalf of the EORTC Quality of Life Study Group. The EORTC QLQ-C30 scoring manual. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer; 2001.
[6] Schwarz R, Hinz A. Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. Eur J Cancer 2001;37:1345–51.
[7] Vergeer MR, Doornaert PA, Rietveld DH, Leemans CR, Slotman BJ, Langendijk JA. Intensity-modulated radiotherapy reduces radiation-induced morbidity and improves health-related quality of life: results of a nonrandomized prospective study using a standardized follow-up program. Int J Radiat Oncol Biol Phys 2009;74:1–8.
[8] Chronowski GM, Garden AS, Morrison WH, Frank SJ, Schwartz DL, Shah SJ, et al. Unilateral radiotherapy for the treatment of tonsillar cancer. Int J Radiat Oncol Biol Phys 2012;83:204–9.
[9] Braakhuis BJM, Visser O, Leemans R. Oral and oropharyngeal cancer in The Netherlands between 1989 and 2006: increasing incidence, but not in young adults. Oral Oncol 2009;45:e85–9.
[10] Little M, Schipper M, Feng FY, Vineberg K, Cornwall C, Murdoch-Kinch CA, et al. Reducing xerostomia after chemo-IMRT for head-and-neck cancer: beyond sparing the parotid glands. Int J Radiat Oncol Biol Phys 2012;83:1007–14.
[11] Levendag PC, Teguh DN, Voet P, van der Est H, Noever I, de Kruijf W, et al. Dysphagia disorders in patients with cancer of the oropharynx are significantly affected by the radiation therapy dose to the superior and middle constrictor muscle: a dose-effect relationship. Radiother Oncol 2007;85:64–73.
[12] Teguh DN, Levendag PC, Voet P, van der Est H, Noever I, de Kruijf W, et al. Trismus in patients with oropharyngeal cancer: relationship with dose in structures of mastication apparatus. Head Neck 2008;30:622–30.
[13] Sinclair CF, McColloch NL, Carroll WR, Rosenthal EL, Desmond RA, Magnuson JS. Patient-perceived and objective functional outcomes following transoral robotic surgery for early oropharyngeal carcinoma. Arch Otolaryngol Head Neck Surg. 2011;137:1112–6.

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