HEAD AND NECK



# Tumor site and disease stage as predictors of quality of life in head and neck cancer: a prospective study on patients treated with surgery or combined therapy with surgery and radiotherapy or radiochemotherapy

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Abstract In this prospective study, we compared the short-term quality of life (QOL) of two subgroups of head and neck cancers: oropharyngeal and laryngeal cancers. Patients treated with curative surgery, were asked to participate in the study using the EORTC QLQ-C30 and H&N35 questionnaires to examine QOL. The oropharynx group consisted of 32 (48 %) patients, while the larynx group consisted of 35 (52 %) patients. All patients were treated with either curative surgery alone or curative surgery combined with adjuvant radiotherapy or radiochemotherapy. The questionnaires were handed out pre- and posttherapy (10 months). At baseline, an impaired overall OOL (=EORTC QLQ-C30 global score) with a value of 53.4 for the whole patient collective was found; the overall QOL after 10 months improved (60.2, p < 0.05). Between the two patient groups, there was no difference in the global score after 10 months. The oropharynx patients described more problems with fatigue and oral cavity associated. The main symptoms in the larynx group were loss of sensual

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function and coughing. The present investigation revealed that the general post-therapy QOL in two subgroups of head and neck cancer reached a satisfying level.

Keywords Head and Neck  $\cdot$  Cancer  $\cdot$  Quality of life  $\cdot$  Oropharynx  $\cdot$  Larynx

# Introduction

Traditionally, oncological studies have focused on survival rates as prime indicators for treatment success. But lately, several studies have been published focusing on quality of life (QOL) instead, such as Hammerlid et al.'s [1, 2] study, which is one of the biggest of its kind.

The World Health Organization defines quality of life as "an individual's perception of their position in life, in the context of culture and value system in their life and in relation to their goals, expectations, standards and concerns" [3]. In recent decades, the number of treatment possibilities has increased significantly through innovations in the fields of surgery, radiotherapy and chemotherapy. However, notwithstanding the amount of treatment possibilities, several studies have shown that the QOL of treated patients is impaired, even if the tumor may be treated successfully [1, 4–9].

This especially applies to the treatment of head and neck cancers [10], which have their origin in several critical organs, such as the spinal cord, brain stem, parotid glands, orbit inner ear and mandible [11]. Treatment can result in severe impairment of physical and social functioning, so a sophisticated analysis of the effects of treatment on QOL is important.

A well-proven method of measuring QOL is the EORTC QLQ-C30 questionnaire and its specific head and neck

cancer module, EORTC H&N-35. Those modules have been validated for clinical use and scientific interpretation in several studies [12, 13] and have been proven to be an important way of communication between the patient and physician. It allows the patient a chance of describing his or her problems and gives the treating physician the means of monitoring the patient's well-being and reaction to symptoms, which would have otherwise gone unnoticed [8]. This may be an important tool to guide future therapeutic decisions and especially applies if the patient has limited means of communication due to his disease or therapy, as many patients with a head and neck cancer experience.

Head and neck cancers are a very heterogeneous group of tumors and a differentiation between the various sites is important, as several studies have found that tumor location can be a predictor of pre- and post-treatment QOL [14, 15]. Patients with an oropharyngeal cancer, especially, are reported to have impaired postoperative QOL. Oropharyngeal cancer is the seventh most frequent type of cancer in males in Germany, with 10,000 new cases diagnosed per year. While most new cases (7,500) are male, within the last decades, the incidence rate for women has increased [16]. Worldwide, the oropharyngeal cancer incidence is rising, with an estimated 200,000–350,000 new cases every year [17]. Approximately 95 % of oropharyngeal cancers are squamous cell carcinomas (SCC), which are often associated with the use of tobacco and alcohol [18].

Tobacco and alcohol use are common risk factors for laryngeal cancer as well, which is the most frequently diagnosed head or neck cancer. It appears primarily in men at a rate of 1.3 % of all cancers in males, as compared to only 0.2 % of cancers diagnosed in women. Apart from the combined use of alcohol and tobacco, there are also certain substances, like nickel or asbestos, which are known to cause laryngeal cancer. In workers who had prolonged exposure to asbestos, laryngeal cancer is acknowledged as an occupational illness [19].

The main aim of our study was to find out if tumor site and stage had an impact on QOL. One of the major goals of the study was to evaluate the QOL of our patients over a short period of time before and after treatment and compare healthrelated QOL between patients with laryngeal and oropharyngeal cancer. Further, we compared various disease stages and examined whether or not other factors had an impact on QOL.

# Materials and methods

Study sample

Between 2008 and 2010, patients diagnosed with oropharyngeal or laryngeal squamous cell cancer were asked to participate in this study. Exclusion criteria included an inability to complete the QLQ C30 and H&N35 questionnaires, severe impairment due to other diseases, and a bad clinical performance status. Of all of the eligible population, 91 patients answered the first questionnaire and 67 patients (mean age 65) filled out the follow-up questionnaire 10 months post treatment. Of the participants, 51 (76 %) patients were male and 16 (24 %) were female.

We divided the patients into two groups, depending on primary tumor site: the Oropharynx group (Group 1) consisted of 32 (48 %) patients, while the Larynx group (Group 2) consisted of 35 (52 %) patients. To examine if stage, as an independent variable, had an impact on QOL, we divided the patients into groups depending on their current tumor stage. Stages I and II were considered to be non-advanced disease and stages III and IV were classified as advanced disease. The first group consisted of 18 patients, while the latter consisted of 49.

All patients received primary surgical therapy, which was intended to be curative. After the surgical treatment, an interdisciplinary tumor board decided the follow-up treatment according to current treatment guidelines. Following the board's suggestions, 50 patients (75 %) received adjuvant therapy. Thirty-two (48 %) were treated with radiotherapy alone, with a cumulative dose of 60–70 Gy (2 Gy single dose) administered over 6 weeks at the primary tumor site. An additional 18 patients (27 %) received adjuvant radiochemotherapy. Following the international guidelines, we used platinum and 5-FU based protocol, in addition to the radiation described above.

#### Methods

The data were collected prior to treatment, as well as at the follow-up care examination that occurred 10 months later. The data include age, tumor stage, grading and histology, smoking or alcohol habits, and HRQOL.

HRQOL was assessed using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire (version 3.0) and the additional EORTC head and neck cancer module, QLQ-H&N35. The EORTC QLQ-C30 consists of five functioning scales (physical functioning, role functioning, cognitive functioning, emotional functioning and role functioning), three symptom scales (fatigue, nausea and vomiting, and pain) and six single items (dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties). There are also two single items concerning global health status and general quality of life. The HQL scores were calculated using the EORTC QLQ-C30 manual. The numbers were transformed into scores ranging from 0 to 100. A high functioning scale score indicates a good level of function; a high symptom scale score represents a high level of symptoms.

The QLQ-H&N35 module was introduced to relate to the more specific symptoms of patients with head and neck cancer. Validated by Bjordal et al. [12] in 1999, it is used in combination with the EORTC QLQ-C30 questionnaire and consists of seven symptom scales (pain, swallowing, problems with senses, speech, trouble with social eating and social contact, and sexuality), as well as 11 single items (teeth, opening mouth, dry mouth, sticky saliva, coughing, feeling ill, weight loss, weight gain and use of feeding tubes, and nutritional supplements and feeding tubes). Here, the scores were also transformed into scales ranging from 0–100, with high scores indicating a higher level of symptoms or more frequent use of painkillers. Scales with missing data were calculated according to the official manual.

#### Statistical analyses and ethics

All data were analyzed using SPSS version 11.5.1 for Windows. We calculated the mean values for each scored item for each of the two evaluation dates. Data were analyzed using a Levene's Test for variance, followed by a paired samples Student's *t* test. We also looked for significant differences depending on tumor staging and localization using the Student's t-test with independent samples. A p < 0.05 was considered statistically significant.

When interpreting data, there can be the problem that statistically significant results represent no clinical difference. Osoba et al. [20] demonstrated that a change of EORTC score of 5–10 is considered as a "little" change, whereas a change of 10–20 points is described as a "moderate" change and a difference of over 20 as "very much". We interpreted our results according to these findings.

The local ethics committee (register number 2958-II) approved the study and all patients gave their consent before inclusion in the study.

#### Results

Patient characteristics and preoperative QOL

The patient characteristics described in the introduction are shown in Table 1. All patients were treated via surgery, either alone or in combination with radiotherapy and/or radiochemotherapy. In the oropharyngeal group, in all patients, we performed a laser-assisted tumor resection. In nine (28.1 %) patients, a defect closure with a radial forearm flap was needed. In the laryngeal group, there were 14 (40 %) limited tumors (T1 and T2), which were resected through an enoral laser-assisted approach. Furthermore, there were 21 (60 %) advanced tumors (T3 and T4), which were treated with a total laryngectomy (TL), and in six (17.1 %) patients, a radial forearm flap was needed for pharyngeal reconstruction. The QOL data at baseline and after 10 months for the study group is shown in Tables 2 and 3.

At baseline, we saw an impaired overall OOL (=EORTC QLQ-C30 global score) with a value of 53.4 for the whole patient collective. The worst function score was emotional function, with a score of 65.3. All other functioning scales showed good results at the time of diagnosis. The worst symptom scales were coughing (41.7), weight loss (44.2), lack of sexual activity (29.5) and pain (26.2). The values for radiotherapy-related symptoms like xerostomia (24.9), sticky saliva (24.6) and speech problems (22.9) were increased. We also saw an elevation of tumor-related symptoms, such as fatigue (24.0), insomnia (26.8) and appetite loss (12.6). Likewise elevated scores were seen for use of painkillers and feeling ill. The patients described only few problems with vomiting (1.9) or diarrhea (1.1), and they had no issues with their sensual function (6.3) or with engaging in social contact (6.3).

In the following passages we will focus on reporting only items that were both statistically significant and clinically meaningful. We decided that according to the findings of Osoba et al. [20] a clinical meaningful scoredifference ( $\Delta$ ) should be at last 10 points.

# Postoperative QOL

The overall QOL after 10 months was better (60.2,  $p < 0.05, \Delta 2.9$ ), although we measured a decrease in all other functioning scales. The scale with the biggest decrease was role functioning (66.9, p < 0.01,  $\Delta - 21$ ). Except for emotional functioning (63.8), these changes were statistically significant and presented a moderate clinical difference. Most symptom scales showed worse scores, with the worst ones being sticky saliva (46.2,  $p < 0.01, \Delta 21.6$ ), dry mouth (45.9,  $p < 0.01, \Delta 20.7$ ), lower sexuality (44.2, p < 0.05,  $\Delta 14.8$ ), dyspnea (43.1, p < 0.01,  $\Delta 21.6$ ) and problems with senses (42.8, p < 0.01,  $\Delta 36.5$ ). Sensual problems and xerostomia showed the biggest differences from the baseline values. The majority of our measurements were statistically significant; the ones showing no significance were coughing, insomnia, pain, constipation, teeth and feeling ill.

The EORTC QLQ-C30 scale for pain was improved (23.3,  $\Delta$ 3.4), but the decrease was small and neither statistically significant nor clinically important. One positive result was that there was significantly less weight loss (20.7, p < 0.05,  $\Delta$ 23.5) and more weight gain (37.9, p < 0.01,  $\Delta$ 31.1).

**Table 1** Characteristics of 67

 patients included in the study

	All	Larynx	Oropharynx
Age			
Mean	64 (45-88)	63 (45-80)	66 (45-88)
Median	62	62	66
Gender			
Male	51 (76.1 %)	28 (80 %)	23 (71.9 %)
Female	16 (23.8 %)	7 (20 %)	9 (28.1 %)
No. of patients	67 (100 %)	35 (52.2 %)	32 (47.7 %)
Stage <sup>a</sup>			
Ι	7 (10.4 %)	5 (14.3 %)	2 (6.3 %)
II	11 (16.4 %)	7 (20.0 %)	4 (12.5 %)
III	10 (14.9 %)	4 (11.4 %)	6 (18.7 %)
IV	39 (58.2 %)	19 (54.4 %)	20 (62.5 %)
Treatment			
Surgery	17 (25.3 %)	9 (25.7 %)	8 (25 %)
Surgery + radiotherapy	32 (47.7 %)	13 (37.1 %)	19 (59.4 %)
Surgery + radiochemotherapy	18 (26.8 %)	13 (37.1 %)	5 (15.6 %)
Surgical treatment			
Oropharynx group			
Laser-assisted resection			32 (100 %)
Radial forearm flap			9 (28.1 %)
Larynx group			
Laser-assisted resection		14 (40 %)	
Total laryngectomy		21 (60 %)	
Total laryngectomy and radial forearm flap		6 (17.1 %)	
Neck dissection			
None	7 (10.4 %)	4 (11.4 %)	3 (9.4 %)
Ipsilateral	20 (29.8 %)	5 (14.3 %)	15 (46.9 %)
Bilateral	39 (58.2 %)	26 (74.3 %)	13 (40.6 %)
Contralateral	1 (1.4 %)	0 (0 %)	1 (3.1 %)
Functional	51 (85 %)	30 (85.7 %)	21 (65,6 %)
Radical	9 (15 %)	1 (2.9 %)	8 (25 %)

<sup>a</sup> UICC classification

# Tumor site

The data for all scores before treatment and after 10 months are shown in Tables 2 and 3, while the additional analysis for the impact of the tumor site is shown in Tables 4 and 5.

Comparing the groups before treatment, the larynx patients described considerably more problems with coughing (48.0 vs. 31.2,  $\Delta 16.8$ ), weight loss (50.3 vs. 32.3,  $\Delta 18$ ) and speech (29.8 vs. 11.5,  $\Delta 18.3$ ) than the oropharynx patients. On the other hand, the patients in the oropharynx group described more pain (24.6 vs. 14.3,  $\Delta 10.3$ ), and thus a heavier use of painkillers (46.9 vs. 20.0,  $\Delta 26.9$ ). In addition, we recorded worse results for some of the symptom scales: opening mouth (19.8 vs. 2.9,  $\Delta 16.9$ ) and dry mouth (33.3 vs. 15.7,  $\Delta 17.6$ ) were the ones showing the clinically most meaningful differences.

There was no considerable difference between both groups for overall QOL after 10 months. The only functioning scale showing a relevant difference was social functioning, and the oropharynx patients had a considerably better score (78.1 vs. 61.4,  $\Delta$ 16.7).

Looking at the symptom scales after treatment, we saw that the Oropharynx group exhibited increased scores postoperations, and hence more problems with oral cavityassociated symptoms, such as dry mouth (55.2 vs. 40), teeth (32.3 vs. 18.1) and opening mouth (34.4 vs. 18.1), which are often related to oral tumor therapy. Interestingly, Oropharynx patients reported increased weight gain (46.9 vs. 28.6) in accordance with a higher use of feeding tubes (28.1 vs. 14.7) and nutritional supplements (21.9 vs. 17.6).

The larynx patients, on the other hand, recorded worse scores for senses (48.6 vs. 29.7), speech (42.4 vs. 20.1) and coughing (46.7 vs. 39.6). Many of the changes from the before treatment (BT) values were statistically significant.

Table 2Mean scores ofEORTC QLQ-C30 at baselineand 10 months

Levene's test and paired Student's *t* tests were used repeatedly to compare the within-group changes at each

NS not significant, suppl.

point of time

supplements \* p < 0.05\* p < 0.01

All groups										
EORTC QLQ-C30	Study group			Oropharynx			Larynx			
	BT	10 months	р	BT	10 months	р	BT	10 months	р	
Quality of life	53.4	60.2	ŧ	54.4	60.4	NS	55.2	61.2	NS	
Physical functioning	83.5	69.8	ş	84.1	68.3	ş	84.5	72.6	ŧ	
Role functioning	81.2	59.2	ŧ	83.9	57.8	ş	81.9	62.9	§	
Emotional functioning	65.3	63.8	NS	68.2	67.4	NS	68.1	64.3	NS	
Cognitive functioning	87.9	75.3	ş	83.9	72.9	ŧ	91.9	79.5	ŧ	
Social functioning	82.5	66.9	ş	84.9	78.1	NS	83.2	61.4	§	
Fatigue	24.0	40.2	ş	24.5	42.7	ş	19.9	33.9	§	
Vomiting	1.9	7.8	ş	2.1	10.9	ŧ	1.4	4.8	NS	
Pain	26.2	23.3	NS	28.1	20.8	NS	21.4	21.9	NS	
Dyspnea	21.1	43.1	ş	23.7	39.6	ŧ	18.1	41.9	ş	
Insomnia	26.8	34.5	NS	28.1	38.5	NS	22.9	28.6	NS	
Appetite loss	12.6	30.5	§	12.5	29.2	NS	10.5	27.6	ŧ	
Constipation	10.4	17.2	NS	14.5	17.7	NS	5.7	15.2	NS	
Diarrhea	1.1	8.6	ş	1.0	6.3	NS	0.9	8.6	ŧ	
Financial difficulties	12.2	31.0	ş	16.1	26.0	ŧ	7.6	32.4	§	

Table 3 Mean scores of QLQ-
H&N35 at baseline and
10 months

All groups										
EORTC QLQ-HN35	Study group			Oropharynx			Larynx			
	BT	10 months	р	BT	10 months	р	BT	10 months	р	
Pain	19	17.9	ŧ	24.6	20.1	NS	14.3	13.9	NS	
Swallowing	16.8	28.3	ŧ	16.4	30.2	ŧ	15.2	27.4	ŧ	
Senses problems	6.3	42.8	ş	7.3	29.7	§	4.8	48.6	§	
Speech problems	22.9	34.6	ŧ	11.5	20.1	ŧ	29.8	42.4	ŧ	
Trouble social eating	12.8	28.4	ş	10.4	29.7	§	12.9	27.2	ŧ	
Trouble social contact	6.3	19.1	ş	3.2	14.6	§	8.0	22.2	§	
Less sexuality	29.5	44.2	ŧ	31.9	46.9	NS	24.2	37.4	ŧ	
Teeth	18.1	25.6	NS	17.8	32.3	NS	16.2	19,6	NS	
Opening mouth	11.7	25.1	ş	19.8	34.4	ŧ	2.9	18.1	§	
Dry mouth	24.9	45.9	ş	33.3	55.2	ŧ	15.7	40.0	§	
Sticky saliva	24.6	46.2	ş	28.1	46.9	ŧ	19.0	46.1	§	
Coughing	41.7	44.8	NS	31.2	39.6	NS	48.0	46.7	NS	
Felt ill	24.6	29.9	NS	22.9	30.2	NS	23.8	26.7	NS	
Use of painkillers	32.6	22.4	NS	46.9	28.1	NS	20.0	17.1	NS	
Nutritional suppl.	4.9	21.1	ŧ	3.1	21.9	ŧ	5.7	17.6	NS	
Feeding tube	3.4	19.3	ş	0	28.1	§	6.1	14.7	NS	
Weight loss	44.2	20.7	ŧ	32.3	18.8	NS	50.3	20.0	ŧ	
Weight gain	6.8	37.9	§	9.7	46.9	§	5.9	28.6	ŧ	

Levene's test and paired Student's *t* tests were used repeatedly to compare the within-group changes at each point of time

*NS* not significant, *suppl*. supplements

 $p^{*} p < 0.05$  $p^{*} p < 0.01$ 

Next, we examined our data for the impact of tumor location on the scales. Results in Tables 4 and 5 show that the differences in social functioning and problems with the senses were significantly related to tumor location. In our study group, patients with a laryngeal cancer clearly had more issues with their olfactory and gustatory function, while patients with oropharyngeal cancer showed a better social functioning.

Independent samples									
EORTC QLQ-C30	Oropharynx 10 months	Larynx 10 months	Advanced 10 months	Non-advanced 10 months	Feeding tube 10 months	No feeding tube 10 months			
Quality of life	60.4	61.2	60.5	59.6	60.6	59.6			
Physical functioning	68.3	72.6	70.9	67.4	72.0	68.9			
Role functioning	57.8	62.9	58.9	59.7	60.6	58.7			
Emotional functioning	67.4	64.3	64.1	63.2	65.2	63.0			
Cognitive functioning	72.9	79.5	74.8	76.3	80.3	73.5			
Social functioning	78.1 <sup>ŧ</sup>	61.4 <sup>ŧ</sup>	67.5	65.8	72.7	65.2			
Fatigue	42.7	33.9	41.3	38.0	35.4	42.0			
Vomiting	10.9	4.8	8.1	7.0	4.5	8.7			
Pain	20.8	21.9	23.1	23.7	13.6	25.7			
Dyspnea	39.6	41.9	41.9	45.6	45.5	43.5			
Insomnia	38.5	28.6	34.2	35.1	33.3	35.5			
Appetite loss	29.2	27.6	33.3	24.6	45.5	27.5			
Constipation	17.7	15.2	18.8	14.0	12.1	18.8			
Diarrhea	6.3	8.6	9.4	7.0	18.2	6.5			
Financial difficulties	26.0	32.4	35.0 <sup>t</sup>	22.8 <sup>t</sup>	39.4	29.7			

Table 4 Mean scores of EORTC QLQ-C30 at baseline and 10 months

Levene's Test and Student's *t* test for independent samples were used to compare the differences at 10 months *suppl*. supplements

 $p^* > 0.05$ 

 $p^{\$} p < 0.01$ 

#### Tumor stage

There are several studies that document a negative association between higher tumor stage and QOL [1, 21–24], so we decided to test our data for a similar effect. Results are given in Tables 4 and 5. For general QOL, as well as the functioning scales, there was no major difference between the two groups. The patients with advanced tumor stages showed higher, albeit not statistically significant higher values on most of the symptom scales. Significant differences were found for financial difficulties (35.0 vs. 22.8), trouble with social eating (35.5 vs. 17.1), placement of a feeding tube (28.9 vs. 5.6), and the use of nutritional supplements (28.9 vs. 5.3). All of the scores mentioned above were elevated for the advanced tumor stages.

# Feeding tube

The placement of a feeding tube is often associated with many problems, such as diarrhea, nausea, local infections and irritated skin around the tube, bleeding, tube obstructions, and leakage, resulting in an impaired HRQOL [15, 23, 25]. Our data showed no significant difference in the general quality of life and functioning scales before treatment and 10 months afterwards. Patients with a placed feeding tube had significantly elevated scales for social

eating (45.5 vs. 23.3, p < 0.01), but on the other hand, they also showed slightly less weight loss (18.2 vs. 21.7, p < 0.05). Of course, patients with a feeding tube used more nutritional supplements (54.5 vs. 13.3, p < 0.05). Surprisingly, the patients with a feeding tube had a better score for pain (10.9 vs. 19.0, p < 0.05) after 10 months.

# Discussion

In this study, we prospectively analyzed the QOL of two subgroups of patients with head and neck cancer. Taken together, oropharyngeal and laryngeal carcinoma account for 5.4 % of all new cancer diagnoses in Germany [19], and about 48.2 % of all squamous cell carcinomas of the head and neck region in comparable countries such as in central Europe and the United States of America [26].

Within the last two decades, a large stream of studies concerning the QOL of patients with head and neck cancer has been published. Recently, So et al. [27] reviewed the literature concerning this issue. They identified 37 studies with moderate to high methodological quality that analyzed the QOL in head and neck cancer patients. In most studies, the emphasis was directed to the post-therapeutic outcome and QOL [27]. One major advantage of our study was to include the pre-therapeutic QOL in interpreting the data.

Table 5         Mean scores of EORTC QLQ-H&N35 at baseline	and 10 months
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Independent samples								
EORTC H&N35	Oropharynx 10 months	Larynx 10 months	Advanced 10 months	Non-advanced 10 months	Feeding tube 10 months	No feeding tube 10 months		
Pain	20.1	13.9	19.9	13.9	10,9 <sup>‡</sup>	19.0 <sup>ŧ</sup>		
Swallowing	30.2	27.4	33.3	17.9	40.2	25.7		
Senses problems	29.7 <sup>§</sup>	48.6 <sup>§</sup>	49.1	29.8	34.8	44.2		
Speech problems	20.1	42.4	33.5	36.8	24.2	36.1		
Trouble social eating	29.7	27.2	33.5 <sup>t</sup>	17.1 <sup>‡</sup>	45.5 <sup>§</sup>	23.3 <sup>§</sup>		
Trouble social contact	14.6	22.2	19.3	18.6	21.2	18.7		
Less sexuality	46.9	37.4	53.3	25.5	59.1	38.8		
Teeth	32.3	19.6	26.1	24.6	21.2	26.7		
Opening mouth	34.4	18.1	27.2	21.1	33.3	22.5		
Dry mouth	55.2	40.0	50.4	36.8	48.5	44.9		
Sticky saliva	46.9	46.1	49.1	40.4	60.6	42.8		
Coughing	39.6	46.7	49.6	35.1	45.5	44.2		
Felt ill	30.2	26.7	29.9	29.8	27.3	31.2		
Use of painkillers	28.1	17.1	28.2	10.5	18.2	21.7		
Nutritional suppl.	21.9	17.6	28.9 <sup>§</sup>	5.3 <sup>§</sup>	54.5 <sup>t</sup>	13.3 <sup>t</sup>		
Feeding tube	28.1	14.7	28.9 <sup>§</sup>	5.6 <sup>§</sup>	Х	Х		
Weight loss	18.8	20.0	20.5	21.1	18.2 <sup>*</sup>	21.7 <sup>t</sup>		
Weight gain	46.9	28.6	38.5	36.8	45.5	34.8		

Levene's Test and Student's t test for independent samples were used to compare the differences at 10 months

§ p < 0.01

When looking at the patient collective as a whole and comparing the values with the EORTC control group of healthy people, the global QOL was reduced. We compared our findings to data collected by Schwarz et al. [28], who performed the QLQ-C30 questionnaire on 2,081 average people. The baseline QOL in our patient group was slightly reduced (65.6 vs. 53.4), and in most functional scales, there was hardly a difference except in the area of emotional function. Here, we saw a severe impairment of 65.3, versus a score of 80.5 for Schwartz's healthy population. So et al. [27] demonstrated that in some studies [29–33], emotional functioning showed the best tendencies towards improvement after 12 months.

Our results, in contrast, could not confirm those previous results. The emotional function was recorded at a constantly low level (63.8) after 10 months. Nevertheless, we saw that in several studies, emotional concerns are recorded as a major issue, and in our center, we already have psychiatrists specializing in psycho-oncology working with our patients. For the symptom scales, we saw elevated values for fatigue, pain, dyspnea, insomnia, appetite loss and constipation in our patient groups. All those were less than 10 points apart from the reference population, so that the clinical difference can be considered to be "little" [20]. When analyzing the specific Head and Neck Module (QLQ-H&N35), the item with the highest score, and hence, the worst QOL, was weight loss. Recently, Hébuterne et al. [34] found out that malnutrition is prevalent in 48.9 % of patients with head and neck cancer. This is supported by data collected by Cacicedo et al. They conducted a prospective analysis of factors that influence weight loss in patients undergoing radiotherapy and showed that having a tumor in the head and neck region was an independent risk factor for weight loss [35].

Gourin et al. [36] emphasized the clinical importance of weight loss for head and neck surgery. In an evaluation of 93,663 cases treated with head and neck cancer surgery, weight loss was associated with increased medical and surgical complications, as well as with longer hospitalization periods and higher hospital-related costs. Ten months after treatment, our patients showed significantly more gain of weight. In particular, the patients with an oropharynx tumor reported about gain of weight. In this group, there was a strong association between weight gain and the placement of a feeding tube and the use of nutritional supplements. Although our patients seemed to benefit with regards to weight gain, a feeding tube was generally reported to be associated with a number of complications

suppl. supplements

p < 0.05

and an impaired HRQOL [15, 23, 25]. This could not be shown for our study group, where the global QOL of patients with a feeding tube was not heavily impaired. Our patients described massive problems with the regular intake of food going along with the fact that eating is a very important aspect to social life. Due to the data obtained by other studies and our study, the routine placement of a feeding tube remains controversial, though there seems to be a positive effect on weight gain. We recommend a feeding tube for the first days after extended surgery of oropharyngeal carcinomas and in patients after TL. If patients develop problems with the oral intake during the postoperative radiation period, the placement of a PEG tube is recommended.

Another increased item at baseline was the use of painkillers. This was even more the case for patients with oropharyngeal cancer. These patients seemed to experience more pain due to the location of their tumor. A comparison of our data to the actual literature is difficult, since in most studies, the pre-therapeutic QOL of life was not reported. Biazevic et al. [37] pre-operatively investigated 47 patients with oropharyngeal cancer concerning their QOL. In their study group they also found pain as one of the items with the worst subjective function. Our data are also in line with the study by Al-Mamgani et al. [38], who evaluated 207 patients with an oropharyngeal cancer and also found that pain was the major baseline complaint of this tumor site.

Our study showed that the general QOL was almost unchanged after therapy for the complete study group as well as for the subgroups (oropharynx or larynx) as compared to the pre-therapeutic value. This finding suggests that the treatment itself did not have a significantly negative influence on the global QOL. Within 10 months after treatment, the general QOL improved slightly in both groups. In contrast to other prospective studies, we could not see a deterioration of the global QOL after treatment.

All other functional items deteriorated within 10 months. In contrast to other studies [27, 29–33] that reported a full recovery in the domains of social, cognitive and role functioning, we could not see such a trend in our study group. De Graeff et al. [39] examined 153 patients with oropharyngeal, hypopharyngeal and laryngeal cancer concerning the QOL after different therapeutic modalities. The baseline emotional functioning was almost similar to our study group (70.4 vs. 68). The authors demonstrated a significant improvement of this domain within 12 months to a value of 81.4.

Regarding the specific head- and neck-related symptoms, we could see problems, especially with senses, speech, dyspnea and social eating. Other major problems for the entire study group were sticky saliva and dry mouth as consequences of the postsurgical adjuvant radiotherapy. As reported by several other studies [29, 30, 40, 41], the symptoms of sticky saliva and xerostomia remained significantly worse at 10 months compared to the baseline.

One major goal of this prospective study was to compare whether or not the tumor site had a major impact on QOL. For this purpose, we compared the development of QOL in patients with oropharyngeal or laryngeal cancers, which are the most common tumor sites in head and neck cancers.

Our study had several very interesting aspects. Concerning the general QOL, there was no significant change between the two study groups. Both groups showed a lower global QOL than the reference data regarding the healthy general German population [28]. Nevertheless, after 10 months of treatment, we could see an improvement in this item for both groups.

Looking at the other items, we could see that the oropharynx patients described heavier oral cavity-associated problems like xerostomia and issues opening the mouth wide. As already mentioned above, those symptoms are generally associated with adjuvant radiotherapy. Recently, there have been many efforts to develop parotid sparing radiation protocols. Increased weight gain and more frequent use of feeding tubes were previously discussed.

The oropharynx group showed a significantly better social functioning reading than did the larynx group. This may be related to the fact that tumor therapy in the oropharynx region is usually less invasive and mutilating. Since the head and neck regions are important to the selfimage and outward appearance of the human being due to their visibility and important functions, such as breathing, smelling, eating and verbal as well as non-verbal communication, highly invasive operations are likely to significantly impair a person's well-being. Encouraging patients to join self-help groups and rely on intact social networks could improve social functioning. As far as our data is concerned, additive therapy for this group of patients should focus on improving xerostomia, for example with saliva substitutes or regular use of mouthwashes, as well as social support. Future therapeutic strategies should try to preserve parotid function as much as possible.

The major problem in patients with laryngeal carcinoma was sensual function. This item remained consistently worse after 10 months as compared to the baseline value. Most of our patients (69 %) in the Larynx group underwent a total laryngectomy (TL) resulting in a disconnection of the upper and lower airways which causes an impairment of the olfactory and gustatory senses. Two other major issues in this group were speech impairment and coughing. Several other studies have shown similar results [42–44].

Because of these complications caused by the loss of the larynx, organ-preserving approaches have become popular and have shown acceptable survival rates [45]. Boscolo-Rizzo et al. compared the HRQOL of patients receiving a TL plus postoperative radiotherapy and primary radiochemotherapy. In their study group, the TL patients had problems similar to our group, while the patients receiving radiochemotherapy reported significantly more problems with their teeth, sticky saliva and dry mouth very similar to the problems described by our patients in the oropharynx group.

Based on the data available, we think that an organpreserving approach (e.g. laser-assisted laryngeal surgery) should be considered and discussed with the patient. In advanced tumors we believe that TL with adjuvant radiotherapy gives excellent survival rates with acceptable QOL. Since the TL still remains the procedure of choice for advanced or recurrent laryngeal cancer, there have been efforts made to optimize the postoperative additive treatment for TL patients. Risberg-Berlin et al. [42] showed the positive effects of the Nasal Airflow-Inducing Maneuver on their patients' olfactory sense, which resulted in a generally high global QOL in comparison to their control group.

Improving the speech function of laryngectomized patients has been a concern of clinicians and researchers for a long time. There have been various speech rehabilitation techniques attempted, and today, the tracheoesophageal voice prosthesis is the gold standard for voice rehabilitation in many centers [46]. It allows for most patients to be able to communicate in a decent manner, resulting in a significant increase in HRQOL.

#### Conclusion

This study documents that the short-term QOL of two groups of patients with head or neck cancer is generally satisfactory compared to a normal population. There was no significant difference according to the location of the tumor. Nevertheless, the subgroups show their therapyrelated problems in specific QOL domains, which may be obscured by general QOL scores. Patients with oropharyngeal carcinoma experience increased levels of pain and complain about xerostomia and sticky saliva, but they also show excellent social functioning and an increased weight gain, which could be associated with more frequent use of feeding tubes. The authors conclude that for this group of patients, post-therapeutic support should focus on improving the oral functions like saliva flow, as well as supporting strategies of good social functioning, for example, in the form of self-help groups. A sophisticated and individually adapted analgesic therapy is a mandatory tool to reach a possibly satisfying QOL.

The QOL of patients with laryngeal cancer was at a good level and improved after treatment, as well. Problems for these patients seem to be mainly associated with the procedure of total laryngectomy, and there have been several interventions to reduce problems with anosmia or taste blindness, as well as verbal inability. Future efforts should be guided in this direction to enable these patients to participate in social interactions as much as possible and to lead a normal life.

Conflict of interest No conflict of interest.

# References

- Hammerlid E, Bjordal K, Ahlner-Elmqvist M et al (2001) A prospective study of quality of life in head and neck cancer patients. Part I: at diagnosis. Laryngoscope 111:669–680. doi:10. 1097/00005537-200104000-00021
- Bjordal K, Ahlner-Elmqvist M, Hammerlid E et al (2001) A prospective study of quality of life in head and neck cancer patients. Part II: longitudinal data. Laryngoscope 111:1440–1452. doi:10.1097/00005537-200104000-00021
- The WHO QOL Group (1994) What quality of life. World Heal. Forum. WHO, Geneva; 1996
- De Boer MF, McCormick LK, Pruyn JF et al (1999) Physical and psychosocial correlates of head and neck cancer: a review of the literature. Otolaryngol Head Neck Surg 120:427–436
- Ledeboer QCP, Velden L-A, Boer MF et al (2005) Physical and psychosocial correlates of head and neck cancer: an update of the literature and challenges for the future (1996–2003). Clin Otolaryngol 30:303–319. doi:10.1111/j.1365-2273.2005.01035.x
- Infante-Cossio P, Torres-Carranza E, Cayuela A et al (2009) Impact of treatment on quality of life for oral and oropharyngeal carcinoma. Int J Oral Maxillofac Surg 38:1052–1058. doi:10. 1016/j.ijom.2009.06.008
- Pourel N, Peiffert D, Lartigau E et al (2002) Quality of life in long-term survivors of oropharynx carcinoma. Int J Radiat Oncol Biol Phys 54:742–751
- Murphy BA, Ridner S, Wells N, Dietrich M (2007) Quality of life research in head and neck cancer: a review of the current state of the science. Crit Rev Oncol Hematol 62:251–267. doi:10.1016/j. critrevonc.2006.07.005
- Oskam IM, Verdonck-de Leeuw IM, Aaronson NK et al (2013) Prospective evaluation of health-related quality of life in longterm oral and oropharyngeal cancer survivors and the perceived need for supportive care. Oral Oncol 49:443–448. doi:10.1016/j. oraloncology.2012.12.005
- Sayed SI, Elmiyeh B, Rhys-Evans P et al (2009) Quality of life and outcomes research in head and neck cancer: a review of the state of the discipline and likely future directions. Cancer Treat Rev 35:397–402. doi:10.1016/j.ctrv.2009.03.001
- 11. Rathod S, Gupta T, Ghosh-Laskar S et al (2013) Quality-of-life (QOL) outcomes in patients with head and neck squamous cell carcinoma (HNSCC) treated with intensity-modulated radiation therapy (IMRT) compared to three-dimensional conformal radiotherapy (3D-CRT): evidence from a prospective randomized study. Oral Oncol 49:634–642. doi:10.1016/j.oraloncology.2013.02.013
- Bjordal BK, Hammerlid E, Ahlner-elmqvist M, et al. (1999) Quality of life in head and neck cancer patients: validation of the European Organization for research. 17:1008–1019
- Bjordal K, Kaasa S (1992) Psychometric validation of the EO-RTC Core Quality of Life Questionnaire, 30-item version and a diagnosis-specific module for head and neck cancer patients. Acta Oncol 31:311–321
- Borggreven PA, Verdonck-de Leeuw IM, Muller MJ et al (2007) Quality of life and functional status in patients with cancer of the

oral cavity and oropharynx: pretreatment values of a prospective study. Eur Arch Otorhinolaryngol 264:651–657. doi:10.1007/ s00405-007-0249-5

- Terrell JE, Ronis DL, Fowler KE et al (2004) Clinical predictors of quality of life in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg 130:401–408. doi:10.1001/archotol. 130.4.401
- Lippman SM, Spitz M, Trizna Z et al (1994) Epidemiology, biology, and chemoprevention of aerodigestive cancer. Cancer 74:2719–2725
- 17. La Vecchia C, Tavani A, Franceschi S et al (1997) Epidemiology and prevention of oral cancer. Oral Oncol 33:302–312
- Talamini R, Bosetti C, La Vecchia C et al (2002) Combined effect of tobacco and alcohol on laryngeal cancer risk: a casecontrol study. Cancer Causes Control 13:957–964
- Koch-instituts R (2012) Krebs in Deutschland Häufigkeiten und Trends Gesundheitsberichterstattung des Bundes Beiträge zur Gesundheitsberichterstattung des Bundes Krebs in Deutschland Häufigkeiten und Trends 07/08 8. Ausgabe 2012
- Osoba D, Rodrigues G, Myles J et al (1998) Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 16:139–144
- Hammerlid E, Taft C (2001) Health-related quality of life in long-term head and neck cancer survivors: a comparison with general population norms. Br J Cancer 84:149–156. doi:10.1054/ bjoc.2000.1576
- 22. Morton RP, Izzard ME (2003) Quality-of-life outcomes in head and neck cancer patients. World J Surg 27:884–889
- Martino R, Ringash J (2008) Evaluation of quality of life and organ function in head and neck squamous cell carcinoma. Hematol Oncol Clin North Am 22:1239–1256, x. doi:10.1016/j. hoc.2008.08.011
- 24. Howren MB, Christensen AJ, Karnell LH, Funk GF (2010) Health-related quality of life in head and neck cancer survivors: impact of pretreatment depressive symptoms. Health Psychol 29:65–71. doi:10.1037/a0017788
- 25. Ronis DL, Duffy SA, Fowler KE et al (2008) Changes in quality of life over 1 year in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg 134:241–248. doi:10.1001/archoto. 2007.43
- 26. Carvalho AL, Nishimoto IN, Califano JA, Kowalski LP (2005) Trends in incidence and prognosis for head and neck cancer in the United States: a site-specific analysis of the SEER database. Int J Cancer 114:806–816. doi:10.1002/ijc.20740
- 27. So WKW, Chan RJ, Chan DNS et al (2012) Quality-of-life among head and neck cancer survivors at one year after treatment—a systematic review. Eur J Cancer 48:2391–2408. doi:10. 1016/j.ejca.2012.04.005
- Schwarz R, Hinz A (2001) Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. Eur J Cancer 37:1345–1351
- Fang F-M, Tsai W-L, Chien C-Y et al (2005) Changing quality of life in patients with advanced head and neck cancer after primary radiotherapy or chemoradiation. Oncology 68:405–413. doi:10. 1159/000086982
- Bozec A, Poissonnet G, Chamorey E et al (2008) Free-flap head and neck reconstruction and quality of life: a 2-year prospective study. Laryngoscope 118:874–880. doi:10.1097/MLG.0b013e318 1644abd
- 31. Ackerstaff AH, Tan IB, Rasch CRN et al (2002) Quality-of-life assessment after supradose selective intra-arterial cisplatin and

concomitant radiation (RADPLAT) for inoperable stage IV head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 128:1185–1190

- 32. Airoldi M, Cortesina G, Giordano C et al (2004) Postoperative adjuvant chemoradiotherapy in older patients with head and neck cancer. Arch Otolaryngol Head Neck Surg 130:161–166. doi:10. 1001/archotol.130.2.161
- Donatelli-Lassig AA, Duffy SA, Fowler KE et al (2008) The effect of neck dissection on quality of life after chemoradiation. Otolaryngol Head Neck Surg 139:511–518. doi:10.1016/j.otohns. 2008.07.007
- 34. Hébuterne X, Lemarié E, Michallet M et al (2014) Prevalence of malnutrition and current use of nutrition support in patients with cancer. J Parenter Enteral Nutr 38:196–204. doi:10.1177/014860 7113502674
- Cacicedo J, Casquero F, Martinez-Indart L et al (2014) A prospective analysis of factors that influence weight loss in patients undergoing radiotherapy. Chin J Cancer 33:204–210. doi:10. 5732/cjc.013.10009
- 36. Gourin CG, Couch ME, Johnson JT (2014) Effect of weight loss on short-term outcomes and costs of care after head and neck cancer surgery. Ann Otol Rhinol Laryngol 123:101–110. doi:10. 1177/0003489414523564
- 37. Biazevic MGH, Antunes JLF, Togni J et al (2010) Survival and quality of life of patients with oral and oropharyngeal cancer at 1-year follow-up of tumor resection. J Appl Oral Sci 18:279–284
- Al-Mamgani A, van Rooij P, Tans L et al (2013) 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? Radiother Oncol 106:359–363. doi:10.1016/j.radonc.2012.12.014
- De Graeff A, de Leeuw JR, Ros WJ et al (2000) Pretreatment factors predicting quality of life after treatment for head and neck cancer. Head Neck 22:398–407
- 40. De Graeff A, de Leeuw JR, Ros WJ et al (2000) Long-term quality of life of patients with head and neck cancer. Laryngo-scope 110:98–106. doi:10.1097/00005537-200001000-00018
- Lloyd S, Devesa-Martinez P, Howard DJ, Lund VJ (2003) Quality of life of patients undergoing surgical treatment of head and neck malignancy. Clin Otolaryngol Allied Sci 28:524–532
- 42. Risberg-Berlin B, Rydén A, Möller RY, Finizia C (2009) Effects of total laryngectomy on olfactory function, health-related quality of life, and communication: a 3-year follow-up study. BMC Ear Nose Throat Disord 9:8. doi:10.1186/1472-6815-9-8
- Boscolo-Rizzo P, Maronato F, Marchiori C et al (2008) Longterm quality of life after total laryngectomy and postoperative radiotherapy versus concurrent chemoradiotherapy for laryngeal preservation. Laryngoscope 118:300–306. doi:10.1097/MLG. 0b013e31815a9ed3
- 44. Leon EA, Catalanotto FA, Werning JW (2007) Retronasal and orthonasal olfactory ability after laryngectomy. Arch Otolaryngol Head Neck Surg 133:32–36. doi:10.1001/archotol.133.1.32
- 45. (1991) Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. N Engl J Med 324:1685–1690. doi:10.1056/NEJM19910 6133242402
- 46. Kapila M, Deore N, Palav RS et al (2011) A brief review of voice restoration following total laryngectomy. Indian J Cancer 48:99–104. doi:10.4103/0019-509X.75841