Original Paper

ORL

ORL 2006;68:253–258
DOI: 10.1159/000093094

Received: February 2, 2005
Accepted after revision: March 26, 2005
Published online: May 4, 2006

Quality of Life after Treatment for Laryngeal Carcinomas

A. Olthoff[a] M.K. Steuer-Vogt[c] K. Licht[d] M. Sauer-Goenen[e] C. Werner[b]
P. Ambrosch[f]

Departments of [a]Otorhinolaryngology and [b]Medical Statistics, University of Göttingen, Göttingen,
[c]Department of Otorhinolaryngology, Technische Universität München, München,
[d]Department of Otorhinolaryngology, University of Regensburg, Regensburg,
[e]Department of Otorhinolaryngology, Medizinische Hochschule Hannover, Hannover, and
[f]Department of Otorhinolaryngology, University of Schleswig-Holstein, Kiel, Germany

Key Words
Laryngeal carcinoma · Partial laryngectomy · Quality of life · Radiotherapy · Total laryngectomy

Abstract
The objective of this study was to evaluate the impact of different surgical treatments as well as of radiotherapy for laryngeal carcinomas on health-related quality of life (QL). In a prospective, randomized multicenter study (five university hospitals in Germany), a total of 146 patients with laryngeal carcinomas (UICC stages: I–IV) underwent different surgical treatments (32 total laryngectomies, 81 CO_2 laser microsurgical partial laryngectomies, 33 open partial laryngectomies). Postoperative radiotherapy was performed in 44 patients. QL data were obtained by using the EORTC QLQ-C30 questionnaire (developed by the European Organization for Research and Treatment of Cancer). Impaired QL data were seen after total laryngectomy and after radiotherapy. Radiotherapy seemed to have more impact on QL than surgical treatment. Global QL was not affected by any treatment. In general, the QL data were not as discriminating as presumed. To evaluate coping abilities, objective measures (voice, swallowing, breathing) should be obtained for comparison in further investigations.

Presented in part at the 72nd Annual Scientific Meeting of the German Society of Otorhinolaryngology, Hamburg, Germany, May 26, 2001.

Introduction

Every laryngeal cancer and its treatment have an impact on the physical, psychological and social health of patients. If patients are able to relate their actual life and health situation (posttreatment) to the situation they had (pretreatment), or want, or expect (fictive), following the 'gap theory', this difference could represent an increase or decrease in health-related quality of life (QL) [1].

In addition to cost analyses, the evaluation of QL after different treatments becomes relevant, provided that the oncological outcomes are comparable [2].

In order to assess health-related QL in cancer patients, irrespective of their specific diagnosis or treatment, a general 'core' questionnaire, called QLQ-C30, was developed and validated by the European Organization for Research and Treatment of Cancer (EORTC) [3]. Later, the EORTC

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0301–1569/06/0685–0253$23.50/0

Accessible online at:
www.karger.com/orl

Arno Olthoff, MD
University of Göttingen, Department of Otorhinolaryngology
Robert-Koch-Strasse 40
DE–37075 Göttingen (Germany)
Tel. +49 551 392 802, Fax +49 551 392 812, E-Mail olthoff@med.uni-goettingen.de

Table 1. Patient characteristics

	All patients (n = 146)	TLE (n = 32)	LPLE (n = 81)	OPLE (n = 33)
Sex				
Male	133 (91)	30 (94)	71 (88)	32 (97)
Female	13 (9)	2 (6)	10 (12)	1 (3)
Age, year				
Median	56	55	57	56
Range	29–70	29–70	38–70	40–68
UICC stage				
I	54 (37)	0	36 (44)	18 (55)
II	37 (25)	2 (6)	25 (31)	10 (30)
III	20 (14)	12 (38)	5 (6)	3 (9)
IV	35 (24)	18 (56)	15 (19)	2 (6)
Tracheotomy	25 (17)	–	1 (1)	24 (73)
Radiotherapy	44 (30)	24 (75)	12 (15)	8 (24)

TLE = Total laryngectomy; LPLE = laser microsurgical partial laryngectomy; OPLE = open partial laryngectomy. Figures in parentheses indicate percentages.

designed and validated a specific 'module' questionnaire for head and neck cancer, the QLQ-H&N35 [4].

However, previous studies often failed to verify significant QL differences in patients with head and neck cancer, comparing surgical and radiotherapeutic treatments or concerning changes over time during or after treatment [5]. Even after total laryngectomy, the impact on QL data was not as distinctive as assumed [2, 6–9].

The aim of our study was to determine the impact of different surgical treatments on QL. For the first time, QL scores of patients treated with endoscopic CO_2 laser microsurgery for laryngeal carcinomas were compared with those of patients who had undergone an open partial laryngectomy or a total laryngectomy. We addressed the question of whether more advanced tumors or more invasive surgery with corresponding functional deficits will affect QL scores in an appropriate manner. The impact of adjuvant radiotherapy was also investigated.

Materials and Methods

Patients

In a prospective, randomized multicenter study, QL data of 443 previously untreated patients with head and neck squamous cell carcinomas (oral cavity, oropharynx, hypopharynx, larynx) were obtained (week 0 to week 156), in order to investigate the outcome after an adjuvant mistletoe extract therapy. Mistletoe extract had not shown either an effect on cancer disease (disease-free survival, 5-year survival rate) or on QL [10].

Of these patients, 177 with laryngeal cancers underwent a primary surgical treatment with curative intention. The aim of this study was to assess the QL impact of tumor stages, different surgical approaches as well as of adjuvant radiotherapy in laryngeal cancer patients. For this purpose, health-related QL data were collected on condition that curative treatment was successful. The observation period was 60 weeks. In order to avoid a tumor disease-related impact on posttreatment QL data, all patients who developed recurrences at local, regional or distant sites or second primary cancers during this period were excluded. In addition, the data of patients who died during this period were not considered, irrespective of the cause of death.

Of all 177 patients, 19 (11%) developed local recurrences during the observation period. Distant metastases were diagnosed in 4 (2%) patients. Eight patients (5%) died. No second primary cancer was observed within this period. After exclusion of these patients (n = 31), all subsequent data refer to the remaining subgroup of 146 patients (table 1).

Total laryngectomy was performed in 32 patients. For partial laryngectomy, 81 patients underwent an endoscopic CO_2 laser microsurgical and 33 patients an open approach. A total of 44 (30%) patients received conventionally fractionated postoperative radiotherapy (2 Gy per day, 5 days per week, median total dose of 60 Gy), to the primary site and both sides of the neck. Radiotherapy started between 8 and 10 weeks after the surgical treatment.

Of the 146 patients (13 females and 133 males), 54 tumors were classified as stage I, 37 as stage II, 20 as stage III and 35 as stage IV in accordance with the criteria of the International Union against Cancer (UICC, 1992) [11]. The mean age was 56 years (range: 29–70 years) (table 1).

QL Assessment

The QLQ-C30 (2nd version) was applied to measure QL scores before (week 0), during (week 8, week 28) and after (week 60) treatment. Later weeks (up to week 156, see main publication) [10] were not analyzed in this study because the immediate impact of different treatments was investigated. These measures should not be influenced by long-term effects of the oncological disease. In addition, missing data increased over time and affected the statistical power. We were unable to use the QLQ-H&N35 because it had not been validated for the German language when we started in 1993.

The QLQ-C30 (with a total of 30 items) includes 5 functional scales (2 items cognitive, 4 items emotional, 5 items physical, 2 items role and 2 items social functioning), 3 symptom scales (3 items fatigue, 2 items pain, and 2 items nausea and vomiting), a global QL scale with 2 items and 6 single items (appetite loss, constipation, diarrhea, dyspnea, financial difficulties, sleep disturbance). According to the EORTC QLQ-C30 scoring manual, all subscales and item scores were linearly converted to a 0–100 scale. For functional and global QL scales, higher scores indicate a higher level, whereas for symptom scales and single items, higher scores represent a lower level of functioning and QL [12].

Statistics

For data analysis, the statistical software SAS (SAS Institute Inc., Cary, N.C., USA) for Windows was used. An extension of the Wilcoxon-Mann-Whitney test for factorial designs with longitudinal data was applied to analyze the time profiles and group effects

Table 2. The influence of different treatments (radiotherapy, surgery) and tumor stages on scales of the EORTC QLQ-C30

	Surgery			Radiotherapy		UICC tumor stages	
	TLE vs. (n = 32)	LPLE vs. (n = 81)	OPLE (n = 33)	RT vs. (n = 44)	NR (n = 102)	III, IV vs. (n = 91)	I, II (n = 55)
Functional scales							
Cognitive functioning		n.s.			n.s.		n.s.
Emotional functioning		+			n.s.		n.s.
Physical functioning		n.s.			n.s.		n.s.
Role functioning		n.s.			n.s.		n.s.
Social functioning		n.s.			n.s.		n.s.
Symptom scales							
Fatigue		+			++		n.s.
Pain		n.s.			+		n.s.
Nausea and vomiting		n.s.			++		n.s.
Single items							
Appetite loss		o			o		o
Constipation		o			o		o
Diarrhea		n.s.			n.s.		n.s.
Dyspnea		o			o		o
Financial difficulties		o			o		o
Sleep disturbance		n.s.			n.s.		n.s.
Global QL		n.s.			n.s.		n.s.

Time profiles and group effects are considered. n.s. = Not significant; + = significant ($p < 0.05$); ++ = significant ($p < 0.01$); o = significant higher-level interaction; TLE = total laryngectomy; LPLE = laser microsurgical partial laryngectomy; OPLE = open partial laryngectomy; RT = radiotherapy; NR = no radiotherapy.

of the scores of the different groups [13]. All interactions were included using a three-factorial design with time-dependent replications. In case of a significant higher-level interaction, a stratified analysis was added. Statistical significance was defined as $p < 0.05$.

Results

As presumed, the highest percentage (94%) of moderately advanced and advanced tumors (stages III–IV) was seen in totally laryngectomized patients. Regarding the patients after partial laryngectomy, stage III-IV disease was seen in 25% of patients who had undergone laser microsurgical treatment and in 15% of patients treated with open partial laryngectomy. A temporary tracheotomy was performed in 1% after endoscopic laser surgery, but in 73% after open partial laryngectomy. Adjuvant radiotherapy was performed in 75% after total laryngectomy, in 15% after laser microsurgery and in 24% after open partial laryngectomy. Details are shown in table 1.

Missing data appeared in several patients and increased over time. They were due to incomplete or missing questionnaires, because many patients came from far away and were followed up by their ENT doctor at home. To exclude a systematic selection of QL data, the values from week 0 were analyzed depending on their presence in the later weeks (weeks 8 and 28, week 60). It turned out that all missing data were missing at random (Wilcoxon test, $p > 0.20$ for 25 of 30 variables and $p > 0.05$ for 5 of 30 variables). In subsequent group comparisons, time profiles and group effects were considered analogously for statistical analyses.

No significant differences in QL scores were detected between the organ-sparing treatments (laser microsurgical or open approach). The circumstance of an open approach with tracheotomy versus a transoral treatment without tracheotomy did not affect QL scores significantly at any time under consideration ($p > 0.05$).

All significant results with respect to the different surgical treatments are due to worse QL scores of totally laryngectomized patients related to patients after laser sur-

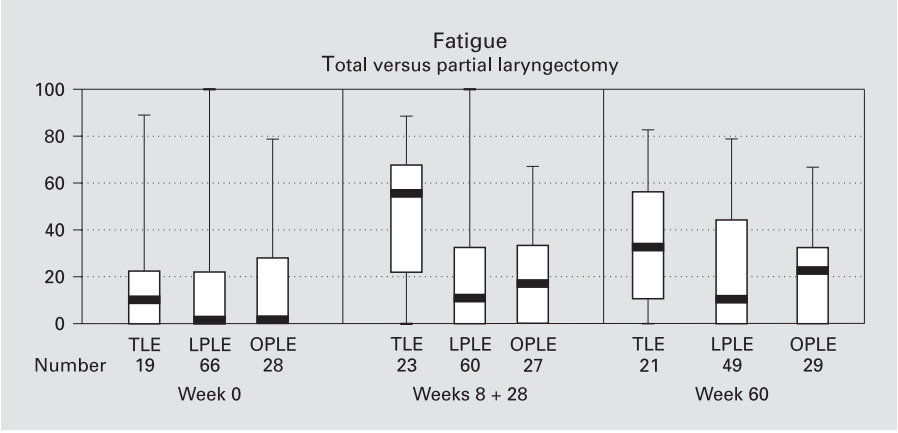

Fig. 1. The values of totally and partially laryngectomized patients differed significantly ($p < 0.05$). Box plot graphs reflect minimum, 25th, 50th, 75th percentiles and maximum. Higher scores represent a lower level of functioning and QL. TLE = Total laryngectomy; LPLE = laser surgical partial laryngectomy; OPLE = open partial laryngectomy.

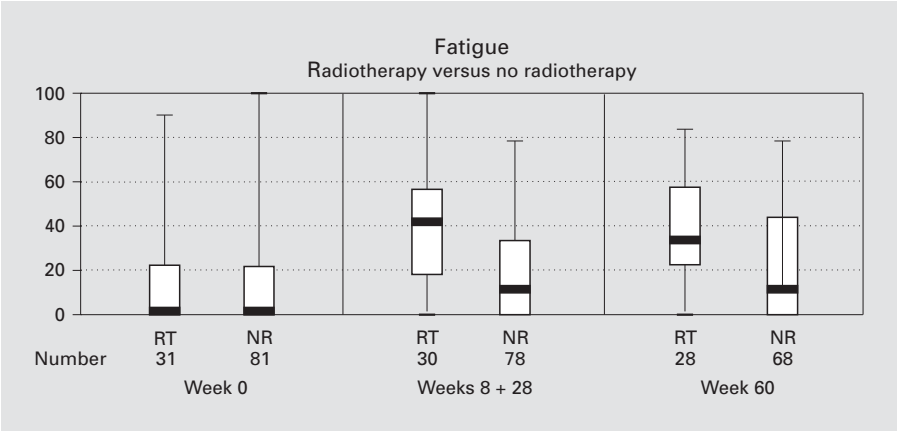

Fig. 2. The values of irradiated and not irradiated patients differed significantly ($p < 0.01$). Box plot graphs reflect minimum, 25th, 50th, 75th percentiles and maximum. Higher scores represent a lower level of functioning and QL. RT = Radiotherapy; NR = no radiotherapy.

gical or open partial laryngectomy. After total laryngectomy, we saw significantly lower values for 'emotional functioning' ($p = 0.047$) and the symptom 'fatigue' was significantly increased ($p = 0.013$). 'Global QL' was not affected (table 2). These deteriorations in totally laryngectomized patients appeared in week 8 and week 28 and persisted up to week 60 (fig. 1).

Comparing the QL data of all patients with ($n = 44$) and all patients without postoperative radiotherapy ($n = 102$), significantly lower QL scores were measured for irradiated patients (table 2). After radiotherapy, we saw a significant increase in the symptom scales: 'fatigue' ($p = 0.006$), 'pain' ($p = 0.035$) and 'nausea and vomiting' ($p = 0.002$) (fig. 2). There was no evident impact of radiotherapy on 'global QL'.

Tumor stages did not show any significant impact on functional scales, symptom scales or single items. Also, 'global QL' was not affected (table 2).

Discussion

The EORTC QLQ-C30 questionnaire is one of the most popular instruments for QL assessment in cancer patients, because of its high specificity, reliability and validity [3]. In our main publication, QL data were obtained up to week 156 after treatment [10]. In this study, only the first 60 weeks were analyzed, because long-term effects of tumor diseases were not to be considered. Furthermore, missing data increased in later weeks, because patients died or avoided traveling long distances from their home to our hospital. This resulted in a decreasing discriminative power of analysis over time. According to the literature, the first year after treatment (surgery, chemotherapy, radiotherapy) is assumed to be the most sensitive period for changes in health-related QL [7, 8].

A significant increase (which indicates lower level of QL) in all symptom scales ('fatigue', 'pain' and 'nausea and vomiting') was seen after radiotherapy. With regard to the surgical treatment, a significant impact on QL

scales was only seen after total laryngectomy with changes in 'emotional functioning' and in the symptom scale 'fatigue'. No significant impact on health-related QL was seen after open partial laryngectomy with tracheotomy in comparison to a transoral laser surgical procedure without tracheotomy. In our study, neither the impact of more invasive surgical treatments (i.e. open approach with tracheotomy), nor the impact of more advanced tumor stages (corresponding to more invasive approaches and pronounced deficits after treatment) were as distinctive as presumed.

Handicaps after surgical treatments seemed to be approved by our patients, but side effects after radiotherapy (stomatitis, xerostomia) might have affected their QL more than surgery did. An impact of radiotherapy, and particularly of xerostomia, on health-related QL has also been seen by others [5, 7, 14].

Previous studies also often failed to verify significant QL differences in patients with head and neck cancer, comparing surgical and radiotherapeutic treatments or concerning changes over time during or after treatment. Regardless of the applied instrument (QLQ-H&N35 in conjunction with the QLQ-C30, University of Washington Head and Neck QLQ, General Health Questionnaire combined with functional single items), the differences revealed were not as distinctive as assumed, even after total laryngectomy [2, 6–8]. When comparing QL after endoscopic CO_2 laser microsurgery versus radiotherapy for early laryngeal carcinomas, no significant differences were seen by Stoeckli et al. [5] in the global QL. However, they saw functional deficits after radiotherapy due to xerostomia.

The QL data obtained are probably influenced by the patients' positive or negative attitude to their therapy. In our study, radiotherapy was performed as an adjuvant approach. In case of poor acceptance, the impact of side effects (i.e. mucositis, xerostomia) on health-related QL might be greater.

The lack of impact after surgical treatments, even when using the ENT-specific module QLQ-H&N35 in addition to the core questionnaire QLQ-C30, in spite of functional deficits (i.e. after tracheotomy), was interpreted in other studies as being due to coping abilities, adaptation to the postoperative situation or posttreatment response shift [6, 7, 15].

This fact may also be based on a traditionally specific relationship between surgeon and patient. In particular, curatively intended surgery might satisfy patients even if functional deficits are unavoidable. A positive attitude to the surgical approach could help patients to overcome disadvantages that arise from their treatment. These patients might adapt to their postoperative situation without an impact on health-related QL.

The missing impact of obviously function-impairing surgical treatments might also indicate optimal pre- and postoperative care and successful rehabilitation. But at least temporary handicaps (breathing, swallowing, voice) cannot be denied and the verification of functional skills by objective measurements becomes mandatory.

The subjective QL scores (functional scales, symptom scales, single items) provide a picture of the impact of different treatments on health-related QL and might help us to understand how patients handle impairments that arise from their disease or its therapy. In addition to oncological data, like survival rate, recurrence rate or disease-free survival, the assessment of QL should be included in oncological study designs, because QL describes one part of the functional outcome after laryngeal cancer treatment [16].

In further investigations, time-related objective tests (videofluoroscopy, body plethysmography, computerized voice analyses) will be added for correlation analyses with the subjective QL scales. This might provide a basis for further investigations of coping abilities. Also by using the QLQ-H&N35 module, ENT-specific symptom scales will be considered and compared to the objective values (swallowing or respiratory disorders, voice quality).

References

1 Morton RP: Evolution of quality of life assessment in head and neck cancer. J Laryngol Otol 1995;109:1029–1035.

2 Morton RP: Laryngeal cancer: quality-of-life and cost-effectiveness. Head Neck 1997;19:243–250.

3 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC: The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365–376.

4 Bjordal K, Hammerlid E, Ahlner-Elmqvist M, de Graeff A, Boysen M, Evensen JF, Biorklund A, de Leeuw JR, Fayers PM, Jannert M, Westin T, Kaasa S: Quality of life in head and neck cancer patients: validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-H&N35. J Clin Oncol 1999;17:1008–1019.

5 Stoeckli SJ, Guidicelli M, Schneider A, Huber A, Schmid S: Quality of life after treatment for early laryngeal carcinoma. Eur Arch Otorhinolaryngol 2001;258:96–99.

6 Finizia C, Hammerlid E, Westin T, Lindstrom J: Quality of life and voice in patients with laryngeal carcinoma: a posttreatment comparison of laryngectomy (salvage surgery) versus radiotherapy. Laryngoscope 1998;108:1566–1573.

7 de Graeff A, de Leeuw JR, Ros WJ, Hordijk GJ, Blijham GH, Winnubst JA: Long-term quality of life of patients with head and neck cancer. Laryngoscope 2000;110:98–106.

8 Weymuller EA Jr, Yueh B, Deleyiannis FW, Kuntz AL, Alsarraf R, Coltrera MD: Quality of life in head and neck cancer. Laryngoscope 2000;110:4–7.

9 Weymuller EA, Yueh B, Deleyiannis FW, Kuntz AL, Alsarraf R, Coltrera MD: Quality of life in patients with head and neck cancer: lessons learned from 549 prospectively evaluated patients. Arch Otolaryngol Head Neck Surg 2000;126:329–336.

10 Steuer-Vogt MK, Bonkowsky V, Ambrosch P, Scholz M, Neiss A, Strutz J, Hennig M, Lenarz T, Arnold W: The effect of an adjuvant mistletoe treatment programme in resected head and neck cancer patients: a randomised controlled clinical trial. Eur J Cancer 2001;37:23–31.

11 Sobin LH: Cancer staging: future directions for the TNM classification. Semin Surg Oncol 1992;8:107–110.

12 Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A: The EORTC QLQ-C30 Scoring Manual, ed 3. Brussels, European Organisation for Research and Treatment of Cancer, 2001.

13 Brunner E, Domhof S, Langer F: Nonparametric Analysis of Longitudinal Data in Factorial Designs. New York, Wiley, 2001.

14 Allal AS, Dulguerov P, Bieri S, Lehmann W, Kurtz JM: Assessment of quality of life in patients treated with accelerated radiotherapy for laryngeal and hypopharyngeal carcinomas. Head Neck 2000;22:288–293.

15 Relic A, Mazemda P, Arens C, Koller M, Glanz H: Investigating quality of life and coping resources after laryngectomy. Eur Arch Otorhinolaryngol 2001;258:514–517.

16 Morton RP: Chemotherapy trials, head and neck cancer, and quality of life. Head Neck 1996;18:92–94.