

Long-term quality of life evaluation after laser microsurgery with or without adjuvant radiotherapy for laryngeal carcinoma

Larenks karsinomu nedeniyle tek başına lazer mikrocerrahisi veya beraberinde adjuvan radyoterapi uygulanan olgularda uzun dönem yaşam kalitesi değerlendirmesi

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Objectives: We evaluated long-term quality of life of patients successfully treated with either laser-assisted microsurgery alone or combined with adjuvant radiotherapy for laryngeal carcinoma.

Patients and Methods: The study included 53 patients who were treated by laser surgery and 16 patients who were treated by laser surgery combined with adjuvant radiotherapy. Quality of life was evaluated with two validated questionnaires: the global EORTC QLQ-C30 and the head and neck specific EORTC QLQ-H&N35. The mean follow-up was 59 months (range 10 to 111 months).

Results: Patients receiving adjuvant radiotherapy showed a significantly lower level of global health status. Surprisingly, the two treatment groups showed close similarities with respect to symptoms specific to the head and neck region. The most frequent complaints were coughing and speech problems in both groups. On the other hand, patients with a follow-up duration of more than or less than five years did not differ significantly with regard to the global health status.

Conclusion: Adjuvant radiotherapy must be selectively utilized in patients treated with laser surgery for laryngeal carcinoma.

Key Words: Laryngeal neoplasms/surgery; laser therapy/methods; quality of life; questionnaires; radiotherapy, adjuvant/adverse effects.

Amaç: Larenks karsinomu nedeniyle sadece lazer mikrocerrahisi veya lazer mikrocerrahisi ile birlikte adjuvan radyoterapi uygulanan olguların uzun dönem yaşam kalitesi sonuçları değerlendirildi.

Hastalar ve Yöntemler: Larenks karsinomu nedeniyle lazer mikrocerrahisi uygulanan 53 hasta ve lazer mikrocerrahisi ile birlikte adjuvan radyoterapi uygulanan 16 hasta çalışmaya katıldı. Yaşam kalitesinin değerlendirilmesinde genel duruma yönelik olarak EORTC QLQ-C30 ve baş-boyun bölgesine yönelik olarak EORTC QLQ-H&N35 formları kullanıldı. Ortalama takip süresi 59 ay (dağılım 20-111 ay) idi.

Bulgular: Genel sağlık durumu bakımından adjuvan radyoterapi uygulanan hastaların daha kötü durumda oldukları saptandı. İlginç bir bulgu olarak, baş-boyun bölgesine özgü semptomlar bakımından iki grup arasında fark izlenmedi. Öksürük ve konuşma sorunları her iki grupta da göze çarpmaktaydı. Ayrıca, uzun dönem (>5 yıl) ve kısa dönem (<5 yıl) takipleri olan hastalar arasında genel sağlık durumu açısından anlamlı fark bulunmadı.

Sonuç: Larenks kanseri nedeniyle lazer mikrocerrahisi uygulanan hastalarda adjuvan radyoterapi verilirken seçici olunmalıdır.

Anahtar Sözcükler: Larenks neoplazileri/cerrahi; lazer tedavisi/yöntem; yaşam kalitesi; anket; radyoterapi, adjuvan/yan etki.

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Squamous cell carcinoma (SCC) of the larynx is the most common malignant tumor of the head and neck region. In 1986, Steiner et al. introduced surgical treatment of early glottic carcinomas using the CO₂ laser.^[1,2] Since that time, laser treatment has developed into an established method not only for laryngeal carcinomas but also for benign laryngeal lesions and vocal cord paralysis.^[3,4] Several authors reported on excellent results with laser-assisted surgery, especially for the treatment of T₁ and T₂ glottic carcinomas.^[2,5-7] Because of the good oncologic results obtained by laser surgery, which are similar to or even better than those obtained by open partial laryngectomy and radiotherapy, this method has developed into a widely accepted alternative treatment.^[1]

Nowadays, the evaluation of successful treatment in head and neck cancers does not only include survival time and disease-free period but also the patients' quality of life (QoL). Especially the treatment of laryngeal cancer has a great impact on breathing and verbal communication. Hence, several authors recently reported on QoL after treatment of laser surgery for laryngeal carcinomas.^[8-11] Since 1986, the European Organisation for Research and Treatment of Cancer (EORTC) has released an integrated system for the evaluation of the QoL of cancer patients. The general EORTC QoL questionnaire (QLQ-C30) contains five functional scales, three symptom scales, and a global health status. A specific module (QLQ-H&N35) has been designed for assessment of QoL in patients with head and neck cancer. Both the core questionnaire and the head and neck module have continuously been validated and re-evaluated.^[12-14]

In this paper, we presented our results concerning QoL in patients who were treated by surgery alone or combined with radiotherapy.

PATIENTS AND METHODS

Design

The study was planned and carried out after completion of therapy and after approval by the ethic committee of the Ruhr University of Bochum. Each patient gave written consent before inclusion into the study. The quality of life questionnaire was explained in detail to the patients and was filled in during the regular outpatient follow-up visit. As a result, 69 patients filled in the questionnaire. Patients with a recurrence, secondary tumors, or

other serious illnesses were excluded. The mean follow-up was 59 months (range 10 to 111 months). The patients were evaluated in two groups based on the treatment performed, i.e., surgery alone (group 1) and surgery followed by radiotherapy (group 2).

Preoperative diagnostic assessment of patients with larynx carcinoma included cervical ultrasonography and computed tomography (CT). All T₃ tumors showed enlarged suspect lymph nodes on CT scans and ultrasonography. In these cases, a neck dissection was performed. All other supraglottic tumors showed no signs of lymphatic metastases in the radiologic diagnosis. "Wait and see" policy was applied for these patients.^[15] Adjuvant radiotherapy was performed for all T₃ tumors. Adjuvant radiotherapy was performed for T₂ tumors when the free margin of tumor resection was below 0.5 cm.

To analyze the long-term quality of life, we further divided the patients into two groups based on the time elapsed from completion of treatment, i.e., less than five years and more than five years.

Questionnaires

For the assessment of the quality of life, we used the EORTC Quality of Life QLQ-C30 German version 3.0 and EORTC QLQ-H&N35, a specific module developed for patients with head and neck tumors.^[12-14]

The EORTC QLQ-C30 consists of six functional scales on physical (5 items), role (2 items), emotional (4 items), cognitive (2 items), social (2 items) and global health (2 items) statuses; three symptom scales on fatigue (3 items), nausea/vomiting (2 items), and pain (2 items); and six single items on dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties. The patients are asked to answer the questions with yes/no responses, or by defining four points from 1 to 4 (1 = not at all, 2 = not much, 3 = moderate, 4 = very much), or on a visual analog scale (1 = very bad to 7 = excellent).

Higher scores for the functional scales represent better quality of life, whereas higher scores on the symptom-oriented scales indicate more severe complaints. The EORTC QLQ-H&N35 consists of 35 questions on symptoms caused by the disease and side-effects of the treatment, for which answers are expected to rate four conditions as in the EORTC QLQ-C30.

Statistical analysis

The data were analyzed using SPSS for Windows version 11.5. For the description of the study groups,

TABLE I
PATIENT CHARACTERISTICS

	Surgery (n=53)	Surgery and radiotherapy (n=16)
Sex		
Male	45	13
Female	8	3
Mean age (years)	65.3	58.4
Tumor location		
Supraglottic	4	7
Glottic	49	9
TNM Stage		
Carcinoma in situ	8	–
T _{1a}	23	–
T _{1b}	15	–
T ₂	7	13
T ₃	–	3
N ₀	53	12
N ₁	–	1
N ₂	–	1
N ₃	–	1
Mean follow-up (months)	61	54
Tracheotomy	1	3

the mean value and standard deviation were determined as descriptive measures. The t-test was used to determine statistical significance for normally distributed values, and Mann-Whitney U-test was used for analysis of variables that were not normally distributed. The level of statistical significance was set at $p < 0.05$ for all tests.

RESULTS

Table I summarizes the clinical details of the participants. The two groups were similar with respect to age distribution and the mean follow-up period. Most patients (n=23) who were treated by surgery alone had T_{1a} glottic carcinoma. All patients who were treated by surgery and radiotherapy had at least T₂ laryngeal carcinoma. The mean follow-up was 61 months in group 1 and 54 months in group 2.

Table II shows the results of the EORTC QLQ-C30 for the two treatment groups, respectively. Concerning the EORTC QLQ-C30 questionnaire, patients who did not receive radiotherapy showed significantly better scores on global health status ($p < 0.01$), and physical ($p < 0.05$) and cognitive ($p < 0.01$)

functioning than those who received adjuvant radiotherapy. On the other hand, patients who received adjuvant radiotherapy showed significant deterioration in seven of nine categories of the symptom scales.

Table III shows the results of the specific EORTC QLQ-H&N35. We found low symptom scores for most items. The highest symptom scores were obtained for speech problems and coughing in both groups without any significant difference. Patients receiving additional radiotherapy experienced significantly more problems with sticky saliva and dry mouth ($p < 0.01$) and sensing problems especially for smell ($p < 0.05$). No significant differences were found between the two treatment modalities with respect to pain, swallowing, social eating, opening of mouth, use of pain killers, and nutritional supplements.

Figure 1 shows the most important mean scores of both EORTC questionnaire modules for patients with follow-up duration of more than five years and less than five years. Patients whose follow-up was less than five years more often complained of constipation and use of pain killers. The two groups were

TABLE II
EORTC QLQ-C30: LASER SURGERY VERSUS
LASER SURGERY AND RADIOTHERAPY
IN LARYNGEAL CARCINOMAS (MEAN±SD)

EORTC QLQ-C-30	Surgery (n=53)	Surgery and radiotherapy (n=16)
Functional scales		
Physical*	82.2±20.2	53.8±29.4
Role	73.2±26.6	44.4±42.7
Emotional	72.3±24.0	65.6±40.2
Cognitive**	83.3±21.1	52.2±30.8
Social	77.5±24.7	63.3±26.1
Global health status**	67.6±18.3	43.3±22.8
Symptom scales/items		
Fatigue**	28.0±24.1	57.7±38.3
Nausea and vomiting**	2.5±7.0	22.2±33.7
Pain**	14.5±26.7	52.2±37.7
Dyspnea	35.5±33.3	60.0±31.4
Insomnia**	27.5±30.9	66.7±43.6
Appetite loss**	13.0±26.7	44.4±43.0
Constipation**	6.5±16.6	35.6±42.7
Diarrhea	3.6±12.7	13.3±27.6
Financial difficulties**	12.3±22.6	46.7±39.4

* $p < 0.05$; ** $p < 0.01$.

TABLE III
EORTC QLQ-H&N35: LASER SURGERY VERSUS LASER SURGERY AND RADIOTHERAPY IN LARYNGEAL CARCINOMAS (MEAN±SD)

EORTC QLQ-H&N35	Surgery (n=53)	Surgery and radiotherapy (n=16)
Pain	8.9±15.3	20.0±26.7
Swallowing	6.7±11.3	26.7±29.7
Sense problems*	7.2±18.1	22.2±31.3
Speech problems	44.7±31.8	36.3±30.4
Social eating	2.5±4.9	19.4±27.0
Social contact	9.6±13.7	16.0±16.3
Less sexuality	32.6±37.8	32.2±31.8
Teeth*	14.5±26.9	31.1±34.4
Opening of mouth	2.2±8.3	2.2±8.6
Dry mouth**	31.8±37.2	75.6±36.7
Sticky saliva**	22.5±35.3	44.4±44.8
Coughing	40.6±34.4	57.8±26.6
Feeling ill	21.7±27.4	44.4±37.1
Pain killers	21.7±41.7	40.0±50.7
Nutritional supplements	4.3±20.6	6.7±25.8
Weight loss	15.2±36.3	40.0±50.7
Weight gain	21.7±41.7	26.7±45.8

*p<0.05; **p<0.01.

similar with regard to global health status. A slight improvement was noted in sensual symptoms.

DISCUSSION

Several authors have demonstrated the efficacy of endoscopic laser resection or radiotherapy in the treatment of laryngeal cancer.^[1,16,17] In this study, we focused on the quality of life of long-term survivors treated with laser-assisted surgery for laryngeal carcinoma. Our data show that the global health status is highly dependent on the treatment modality. The patients treated with additional radiotherapy exhibited significant impairment in their global health status. As reported by Olthoff et al.^[18] the symptom 'fatigue' differed significantly between irradiated and nonirradiated patients. Concerning the surgery group, our results were consistent with those reported in the literature.^[17,19] Physical and cognitive functions were more likely to be impaired in patients to whom adjuvant radiotherapy was administered following laser surgery.

Functional scales of the EORTC QLQ-C30 showed highly significant differences in the assessment of

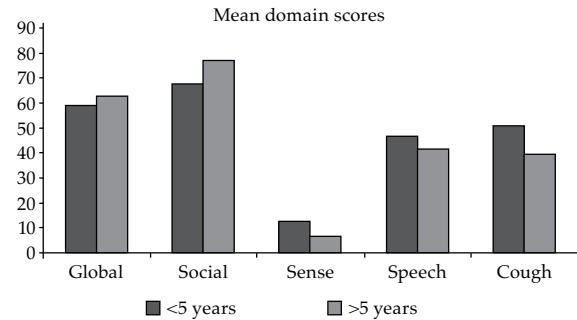


Fig. 1. Comparison of the mean domain scores of patients based on the length of follow-up.

global health status, cognitive functioning, and symptom scales. Ohlwein et al.^[11] reported similar results with a slightly better global health status in patients undergoing minimal invasive laser surgery.

The ENT-specific EORTC QLQ-H&N35 interestingly showed very few differences between the two treatment modalities. Irradiated patients showed typical symptoms, such as dry mouth and sticky saliva, which were caused by the therapy. Coughing was one of the major problems in both groups. Although patients receiving additional radiotherapy had larger tumors and more excision of laryngeal tissue, the majority of the items on the EORTC QLQ-H&N35 did not show significant differences between the two treatment modalities.

As previously reported, speech problems were also one of the major complaints.^[11] Problems with senses especially concerning smell were mentioned by patients who were treated with additional radiotherapy. Recently Bindewald et al.^[20] who reported from a re-analysis of two multi-institutional cross-sectional studies found that postoperative radiotherapy had the highest impact on the patients' QoL irrespective of other clinical factors following surgery for laryngeal carcinoma.

In our study, nausea-vomiting, pain, insomnia, loss of appetite, constipation, and financial problems were the global problems that existed more frequently in patients receiving adjuvant radiotherapy.

The indicators of quality of life seemed to be independent of the length of follow-up after completion of treatment. Even though patients whose length of follow-up was more than five years showed slightly better results in the items of global health status and social functioning, there were no significant differences in the main symptoms like coughing

and speech after laser-assisted surgery. Especially, it is expected that coughing and speech problems should improve over time. In contrast to previous reports, ^[19,21] the quality of life of our patients was not dependent on the time passed after completion of treatment. These results emphasize the need for multidisciplinary coordination to handle the problems that may impair the quality of life in patients with larynx cancer.

In conclusion, our study showed that patients treated with surgery alone showed better global health status and a lower symptom profile than those receiving adjuvant radiotherapy. Therefore, adjuvant radiotherapy must be selectively used in patients treated with laser surgery for laryngeal carcinoma.

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