Quality of life following endoscopic resection or radiotherapy for early glottic cancer

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ABSTRACT

Objective: To compare post treatment quality of life (QoL) of patients treated by radiotherapy or endoscopic transoral endolaryngeal surgery using two quality of life scoring tools.

Methods: From May 1998 to July 2005, 48 patients (11 women and 37 men) with early glottic cancer were treated with curative radiotherapy (18 patients) or laser cordectomy (30 patients), and retrospectively evaluated using QoL questionnaires; European Organization for Research and Treatment of Cancer (EORTC) - EORTC-QoL Core Questionnaire (QLQ-C30 version 2.0) and organ specific EORTC - QLQ, Head and Neck Module (QLQ-H&N35) at the University Hospital Motol, Czech Republic.

Results: Mean follow-up was 24 months. Only patients in complete remission were enrolled in the study. The overall score calculated separately for both questionnaires was not statistically different between both groups. Statistically significant differences were found only in specific group of questions focusing on saliva production (p=0.034) and sexuality performance (p=0.002). The majority of cases treated with cordectomy were Tis lesions. In the radiotherapy group, T1 lesions predominated (p=0.0001). Patients treated with radiotherapy were significantly older than those treated with cordectomy (p=0.027), which could explain the worsened score in sexuality questions. There were no significant differences found between genders allocated either to cordectomy or radiotherapy group.

Conclusions: The overall QoL did not differ between patients treated with cordectomy or radiotherapy, despite the fact that patients treated with radiotherapy had more advanced disease and were older. There was significantly worse saliva and sexuality question score in the radiotherapy group.

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Laryngeal cancer is considered the most common cancer of the upper aero-digestive tract. It is in tight relation to both passive or active smoking and alcohol abuse. Majority of these patients, especially those with glottic cancer, have early warning symptoms like hoarseness and other voice changes and thus, are often diagnosed with early-staged laryngeal cancer, described as T1N0M0 or T2N0M0.[1] Although being a malignant disease, early-staged laryngeal cancer has a very good prognosis with a high 5-year overall survival, disease specific survival and local control rates regardless of the treatment modality used.[2-5] There is still some controversy regarding the treatment of choice, however, a single-modality strategy is generally accepted. Radiotherapy was considered the golden standard of treatment for several decades, however, the introduction of minimally invasive endoscopic techniques and medical lasers has changed the situation. Now, the preferred treatment varies in different countries, radiotherapy is the therapy of choice in northern Europe, Australasia, and Canada, while surgery is prevalently used in southern Europe and many centers in the United States.[6]

The full list of treatment options includes radiotherapy with standard regimens, external (vertical partial laryngectomy or supracricoid laryngectomy with crico-hyoido-pexy) or endoscopic laser-assisted surgery. There are also promising studies using photodynamic therapy.[7] All of the mentioned modalities yield similar rates of local control, overall, and disease specific survival. When the disease can be treated by different modalities with the same oncological results, other endpoints of therapy have to be evaluated for proper

treatment selection. Since the patient's quality of life (QoL), quality of voice, and direct and indirect cost of treatment have emerged as very important endpoints of management of the early laryngeal cancer. The type of treatment is chosen after various factors like the location of tumor, its size and depth of infiltration and patient's co-morbidities are analyzed, but also, the philosophy of the physician and institution and the patient's wishes play a very important role in treatment decision-making. Overall, the most appropriate treatment should be based on a multidisciplinary approach.

The aim of this study was to compare post treatment QoL of patients treated by radiotherapy or endoscopic transoral endolaryngeal surgery using two QoL scoring tools.

Methods. From May 1998 to July 2005, 48 patients with early glottic cancer stage Tis (17 patients), stage T1a (26 patients), stage T1b (4 patients) and stage T2 (1 patient) were treated with laser cordectomy (30 patients) or curative radiotherapy (18 patients), and retrospectively evaluated using QoL questionnaires; European Organisation for Research and Treatment of Cancer (EORTC) - EORTC-QoL Core Questionnaire (QLQ-C30; version 2.0)[12,13] and organ specific EORTC QLQ, Head and Neck Module (QLQ-H&N35) at the University Hospital Motol, Czech Republic. The mean follow-up time was 24 months. At the time of questionnaire evaluation, the median age of cordectomy patients was 60 years (range 29-81 years) and the median age in radiotherapy group was 69 years (range 53-85 years). There were 11 women (23%) and 37 men (77%) included in the study. Pre-treatment evaluation included history and physical examination, baseline hematology and biochemistry, chest x-ray, microlaryngoscopy, and biopsy taken under general anesthesia. Patients treated with radiotherapy were irradiated using linear accelerator with computed tomography localization of target volume. In all patients, radiotherapy was performed according to the International Commission on Radiological Units and Measurements (ICRU) guidelines[8] in 2 Gy daily fractions, 5 days per week. Three dimensional, conformal (3D) treatment planning was employed. Treatment volume included the primary tumor site with dose to the primary 66 Gy in stage Ia, and 70 Gy in stage Ib and II disease. Isocentric technique of 2 anterior oblique fields was used. High-energy photon beams 4 megaelectronvolt (MV) or 6 MV were used. Laser surgery was performed in accordance with type I-III cordectomy technique described and classified by some studies (namely, subepithelial cordectomy/type I: resection of the epithelium; subligamental cordectomy/type II: resection of the epithelium, Reinke's space and vocal ligament; transmuscular cordectomy/type III: resection through the vocalis muscle).[9-11] Scales of QLQ-C30 consists of function scales; physical function, role function, social function, emotional function, cognitive function, global health status, and QoL, symptom scales and single item include; fatigue, pain, appetite loss, nausea, vomiting, dyspnea, sleep disturbance, constipation, diarrhea, and financial difficulties. Scales of QLQ-H&N35 were pain, swallowing, senses, speech, social eating, social contact, sexuality, teeth problems, trismus, dry mouth, sticky saliva, coughing, feeling ill.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows version 10.0 (SPSS Inc., Chicago, USA), *p*-values of less than 0.05 were considered to indicate statistical significance. Quality of life was evaluated with the non-parametric Mann-Whitney test. Fisher's exact test was used for categorical data.

Results. Mean follow-up was 24-month (1-89 months). Only patients who were in complete remission after initial treatment were assessed. The return rate of the answers was 90%. The overall score calculated separately for both questionnaires was not statistically different between the group treated with cordectomy or radiotherapy (p=0.798 for the QLQ-C30 and p=0.991 for the QLQ-H&N35 questionnaires) (**Table 1, Figures 1 & 2**). Statistically significant difference were found only in specific group of questions focusing on saliva production (p=0.034) and sexuality performance (p=0.002). Grouping of the parameters of EORTC QLQ-C30 to physical activities, role, emotional, cognitive score calculated for both questionnaires separately were not statistically different between the groups treated with cordectomy or radiotherapy. Results in questions in EORTC QLQ-H&N35 questionnaire focusing on pain, swallowing, senses, speech, social contact, sexuality, teeth problems, trismus, dry mouth, saliva, cough, feeling ill were without statistical differences between the groups treated with cordectomy or radiotherapy. The majority of cases

Table 1 - Differences in mean score of the QLQ-H&N 35 and QLQ-C30 by treatment status.

Questionary	Treatment modality	n	Mean ± SD	SEM
QLQ-C30	Cordectomy	30	45.47 ± 5.077	0.927
	Radiotherapy	18	48.94 ± 12.753	3.006
QLQ-H&N35	Cordectomy	30	39.33 ± 7.298	1.332
	Radiotherapy	18	42.56 ± 13.682	3.225

SD - standard deviation, SEM - standard error of mean,

treated with cordectomy were Tis lesions (57%). In the radiotherapy group T1 lesions predominated (100%) (p=0.0001). Patients treated with radiotherapy were significantly older than those treated with cordectomy (p=0.027) which could explain the worsened score in sexuality questions. There was no significant difference found between genders allocated either to cordectomy or radiotherapy.

Discussion. The primary objective of this retrospective study was to evaluate the post-treatment QoL of patients undergoing a single modality surgical or curative radiotherapy for the early stage glottic laryngeal carcinoma (T1N0, T2N0). All the data obtained were based on patient's self-evaluation. We used two QoL questionnaires developed by the EORTC - EORTC-QoL Core Questionnaire (QLQ-C30; version 2.0), and organ specific EORTC QLQ, Head and Neck Module (QLQ-H&N35).[14] It is known that those instruments must be designed as multidimensional tools providing the possibility to perform a cross-sectional analysis of patients' QoL and treatment sequel. Even with the most sophisticated QoL instruments, it is very difficult to obtain really representative and more important reproducible data. It is obvious that patients with different tumors react diversely to different treatments, but also in such a relatively homogenous population like in the present study with quite similar tumor location and tumor extent the patient's QoL self-evaluation can be surprisingly high or low.[15] The return rate of questionnaires in present study was 90%, which is higher than the usual return rate given for questionnaire surveys in the literature.[16] Consistently with other studies, both treatment modalities yielded a

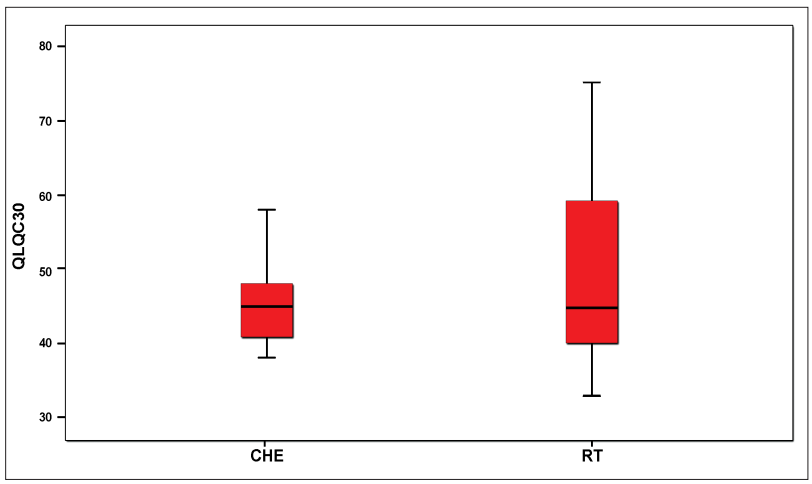

Figure 1 - Overall scores for QLQ-C30 boxplots according to cordectomy (CHE) or radiotherapy (RT) (p=0.798).

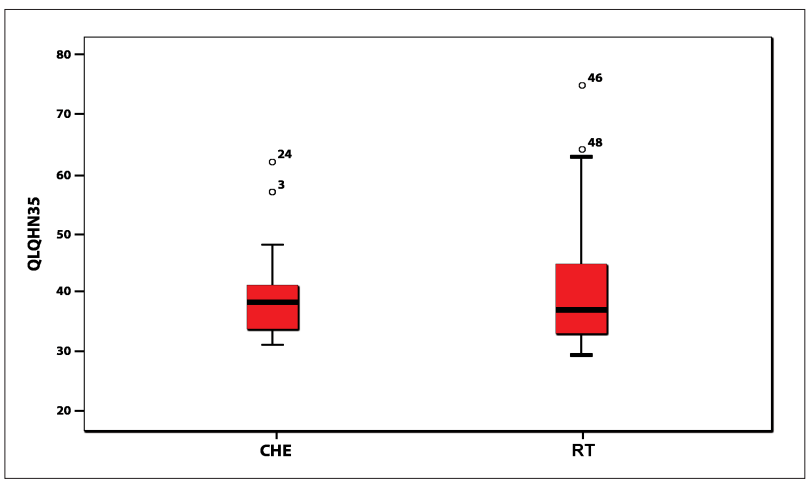

Figure 2 - Overall scores for QLQ-H&N35 boxplots according to cordectomy (CHE) or radiotherapy (RT) (p=0.991).

relatively high overall QoL scores, with a mean global health status in both groups around 70%.[17] Functional domains (cognitive, emotional, role functioning, and so on) revealed almost normal percentages. Patients treated with radiotherapy had significantly worse sexuality domain scores (p=0,002). The fact that patients in the radiotherapy group were older than in the surgically treated group could theoretically explain this result. The tumor site related symptom scores, obtained by the QLQ-H&N35 questionnaire, were low for majority of items throughout the cohort which document the low immediate and long-term side effects of both treatment modalities.

Although, both treatment modalities should adversely affect speech, there was no statistically significant difference between the two modalities, the voice of surgically treated patients was not rated worse than in the radiotherapy group. There is still some controversy regarding the method of voice self-assessment. The results of this study contrast with some objective studies, showing that the voice post-treatment quality is poorer in the surgically treated patients.[18,19] Conversely, McGuirt et al[20] compared two groups of a higher selected patients treated by radiotherapy or endoscope surgery, and found no significant differences in voice quality when tumor volume was small, the voice quality in surgically treated patients is the function of the amount and type of tissue excised. These findings were confirmed by several other studies.[21] In the study of Brandenburg,[22] he described the predominant vocal feature after tumor excision as breathiness, while harshness and raspiness was typical vocal impairment after radiotherapy. The assessment of speech problems by QoL tools based on patients voice self evaluation does not seem to be sensitive and efficient enough, which was shown in study published by Muller.[16] The well-known negative side effect of radiotherapy on swallowing can be seen in the present study. The typical post radiotherapy head and neck specific symptom is sticky saliva. It was the only symptom found significantly different and worse in the radiotherapy group. The explanation of this fact is that, irradiation of minor salivary glands in the laryngeal mucosa and surrounding tissue plays important role in saliva quality (major salivary glands were not irradiated) and the other explanation could be the cohort demographic description (patients in radiotherapy group were significantly older and thus had fewer reserves and lesser organ restoration capacity). It could be roughly extrapolated that this symptom affects QoL in patients treated for early staged glottic cancer more than voice function and is often underestimated.[23] According to the latest findings, the data obtained from the QoL assessment contribute to the facilitation and improvement of the communication between the physician and the patient than the influence of the therapy and its outcomes. But recently, published research results show that (more in context with chemotherapy) patients with impaired QoL are not only more likely to experience marked side effects of therapy, however, that QoL could furthermore provide independent prognostic information.[24]

In conclusion, the overall QoL evaluated according to Quality of Life questionnaires, EORTC QLQ-C30 (version 2.0) and EORTC QLQ-H&N35 did not differ between patients treated with cordectomy or radiotherapy despite the fact that patients treated with radiotherapy had more invasive disease and were almost 10 years older. In particular questions, there was significantly worse saliva and sexuality question score in the radiotherapy study arm. In the future, all used instruments should be standardized and it is clearly visible, that there is need to narrow the range of QoL evaluation tools. This should provide the relatively objective and reproducible data with the possibility to exchange and to compare them between the oncological centers. For better evaluation of voice post-treatment changes, specific diagnostic tools like Voice Handicap Index questionnaire should be employed, and furthermore correlated with the results of objective voice analysis. Survivors' QoL should be implanted as a common part of prospective randomized trials.

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