ORIGINAL ARTICLE

Quality of life in patients treated for advanced hypopharyngeal or laryngeal cancer

M. Guibert a, B. Lepage b, V. Woisard a, M. Rives c, E. Serrano a, S. Vergez a,∗

a Service d’ORL et chirurgie cervico-faciale, CHU de Toulouse, hôpital Rangueil-Larrey, 24, chemin de Pouyvourville, 31059 Toulouse cedex 9, France
b Service de biostatistiques, CHU de Toulouse, 31059 Toulouse cedex 9, France
c Service de radiothérapie, institut Claudius-Regaud, 20/24, rue du Pont-Saint-Pierre, 31052 Toulouse cedex, France

Available online 25 May 2011

KEYWORDS
Quality of life; Pharyngeal and laryngeal squamous cell carcinoma; Total (pharyngo-) laryngectomy; Organ conservation

Summary
Objective: To study quality of life in patients treated for advanced hypopharyngeal or laryngeal cancer, with laryngeal conservation or laryngectomy.
Patients and methods: A retrospective 2-center study included 100 patients in remission from squamous cell carcinoma, treated between 1998 and 2009. Seventy patients (24 hypopharynx, 46 larynx) were treated by total (pharyngo-) laryngectomy followed by external radiation therapy, and 30 (13 hypopharynx, 17 larynx) underwent an organ-conservation protocol with concurrent radiochemotherapy or with induction chemotherapy using platin-5FU or taxan-platin-5FU followed by radiation therapy. All patients responded to the quality of life questionnaires (EORTC QLQ-C30 and QLQ-H&N35).
Results: Advanced tumor stages IVA and IVb were significantly more frequent in the surgery groups (hypopharynx: 71.6% vs. 45.9%, p = 0.01; larynx: 72.4% vs. 37.5%, p < 0.01). In pharyngeal cancer, the only significant difference between surgical treatment and laryngeal conservation was for ‘sensory disorder’ (taste and odor), with better results in case of laryngeal conservation (p < 0.0001). For the other items, there was a trend for quality of life to appear better in patients with laryngeal conservation (p = NS). In laryngeal cancer, the only significant difference was for ‘dry mouth’, which was significantly less invalidating with surgical treatment (p < 0.001). The impairment of the other quality of life items did not differ between surgical and conservative treatment.
Conclusions: Quality of life is impaired in all patients treated for pharyngeal or laryngeal cancer. The type of treatment, surgical or conservative, affects differently various aspects of quality of life.
© 2011 Elsevier Masson SAS. All rights reserved.

Introduction
Curative treatment of advanced-stage laryngeal and hypopharyngeal squamous cell carcinoma classically
Quality of life in patients treated for advanced hypopharyngeal or laryngeal cancer

consists in total (pharyngo-) laryngectomy, resulting in definitive tracheostoma and voice loss. The alternative to this mutilating attitude is concurrent or sequential radiochemotherapy, conserving the pharyngolaryngeal organ. Its feasibility and efficacy in organ conservation and oncologic control have been demonstrated [1–4]. However, these studies did not assess patient quality of life (QoL), simply trusting that not sacrificing the larynx is bound to be good for QoL. Yet the secondary effects of chemotheraphy and radiation probably also impair QoL. The present study therefore compared QoL in advanced pharyngeal and laryngeal cancer patients managed on an organ-conservation protocol or by total (pharyngo-) laryngectomy followed by external radiation therapy.

**Patients and methods**

**Population characteristics**

One hundred and eleven laryngeal or hypopharyngeal squamous cell carcinoma patients treated between 1998 and 2009 and currently in clinical remission were included in a retrospective study. Locoregional or remote evolution or recurrence were exclusion criteria. Treatment by total (pharyngo-) laryngectomy or on an organ-conservation protocol was decided upon in a multidisciplinary coordination meeting.

Total laryngectomy was systematically backed up by external radiation therapy (44–75 Gy), with adjuvant chemotherapy in 31 patients. Successive organ-conservation protocols were implemented over the study period: platinum-5fluorouracile (PF) induction chemotherapy, concurrent radiochemotherapy, and docetaxel-platinum-5fluorouracile (TPF) induction chemotherapy. Induction chemotherapy was followed by external radiation therapy in responsive patients. Patients initially managed by induction chemotherapy but then undergoing salvage laryngectomy were included in the surgery group.

Sixty-three of the 69 laryngeal cancer patients filled out the QoL questionnaire. Forty-six had undergone total laryngectomy and 17 an organ-conservation protocol (three by PF, 10 by TPF and four by concurrent radiochemotherapy). Thirty-seven of the 43 hypopharyngeal cancer patients filled out the QoL questionnaire. Twenty-four had undergone total laryngectomy and 13 an organ-conservation protocol (six by PF, five by TPF and two by concurrent radiochemotherapy). Two laryngeal cancer patients who had received conservative treatment underwent tracheotomy. There were no cases of gastrostomy. The study was thus finally performed on 100 patients. For the two locations taken together, tumors were mainly stage III (29%) or IVa (56%). The QoL questionnaire was sent to the patients least 1 year after treatment termination, and responses were collected by mail, in consultation or by telephone.

**Quality of life assessment**

The study used the European Organization for Research and Treatment of Cancer (EORTC) questionnaire. This consists of a generic section (QLQ-C30) comprising six functional scales (physical, social, emotional, cognitive, role and general status), three symptom scales (fatigue, pain, nausea and vomiting) and six independent items (dyspnea, insomnia, appetite, constipation, diarrhea and financial difficulties). The specific head and neck cancer module (QOL-H&N35) comprises seven symptom scales (pain, swallowing, senses, speech, social eating, social contact and sexuality) and nine independent items (teeth, opening mouth, dry mouth, thick saliva, cough, feeling ill, pain killers, nutritional supplements, feeding probe and weight gain and loss). Each scale and item is scored 0–100 after linear transformation. The functional scale scores are inverse: i.e., the higher the score, the better the function; on the symptom scales and independent items, the higher the score, the greater the difficulties or symptoms.

**Statistical analysis**

Data were collected separately for laryngeal and hypopharyngeal cancer patients. Analysis used Stata SE 11.0 software. Quantitative variables were described as mean, standard deviation and median. Qualitative variables were described as number and percentage. Demographic and medical variables were compared between treatment groups by Khi², Fisher’s exact or Student t test. QoL scores were compared between groups by Wilcoxon or Fisher’s exact test with Bonferroni correction. The significance threshold was set at p < 0.0015.

**Results**

**Laryngeal cancer**

Patients in the organ conservation group tended to be younger, but without significant difference. Stage IV was significantly more common in the surgery group (p < 0.002) (Table 1). The median interval between end of treatment and response to the QoL questionnaire was 3 years (in both groups: range, 12 months to 11 years).

Responses on the generic questionnaire (C30) showed no significant differences according to treatment group (Table 2). The trend most closely approximating significance was on the independent item “insomnia” (p = 0.04) (Fig. 1), with higher scores in the surgery group: 33 point difference between the medians of the two groups.

Responses on the specific questionnaire (H&N35) showed a significant difference on the independent item “dry mouth” (p < 0.001), with higher scores in the conservative group (Fig. 1). Another difference approximating significance (p = 0.02) was on the “sticky saliva” item, with a tendency toward greater severity in the conservative group: 33 point difference between the medians of the two groups. The difference in medians between the two groups was 50 points on the “senses problems” item, with a tendency toward greater severity in the surgery group, although this result did not reach significance (p = 0.02). On the other specific questionnaire items, there were no significant differences according to treatment group.
### Hypopharyngeal cancer

Hypopharyngeal cancer showed the same age and tumor-stage distributions as laryngeal cancer (Table 1).

The median interval between end of treatment and response to the QoL questionnaire was 4 years (range, 12 months to 11 years): 3 years 5 months in the surgery group, and 4 years 2 months in the conservative group.

On the generic questionnaire, there were tendencies toward significance on the “general status” ($p = 0.10$), “physical functioning” ($p = 0.07$) and “emotional functioning” ($p = 0.05$) scales, in the direction of better quality of life in the conservative group (differences between median scores: 17, 7 and 24 points, respectively) (Table 2). On the other questionnaire items there were no significant differences according to treatment group.

Responses on the specific questionnaire showed a significant difference on the “sensory problems” item ($p < 0.001$), with greater severity in the surgical group and a 66 point difference between the medians. Another difference approximating significance was on the “social eating” item ($p = 0.02$), with a tendency toward greater difficulty in the surgery group: 37 point difference between medians (Fig. 2). On the other questionnaire items there were no significant differences according to treatment group, although the distribution of scores tended fairly systematically to be in favor of the conservative group. Weight gain tended to be more often observed in the conservative group (54% vs. 21%), although the difference did not reach significance ($p = 0.07$).

### Discussion

Assessment of change in quality of life in head and neck cancer used to be restricted to voice and swallowing disorders [5]. More complete measurement tools have now been available for a number of years, enabling overall QoL impact to be assessed. QoL questionnaires are of two sorts: generic and specific [6]. Generic tools assess the overall impact of health status, covering global functional dimensions such as the physical, social and psychological domains. Their drawback lies in their failure to spotlight particular aspects of certain pathological processes. Specific tools can compare patients with a given pathology, and their sensitivity enables change in cancer patients’ health status to be detailed over time. Assessment of head and neck cancer treatment effects requires specific tools, given the specific disorders of voice, swallowing and sensation as well as issues of physical appearance induced in these patients. For certain treatments, such as radiation therapy, specific tools have been developed to assess consequences [7].

The present study used the EORTC QoL questionnaire, comprising a generic (QLQ-C30) [8] and head and neck cancer-specific section (QLQ-H&N35) [9]. Its validity and specificity have been demonstrated. Combined use of the two sections has been validated in a study of head and neck

---

### Table 1 Demographic characteristics of patient subgroups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Larynx</th>
<th>Hypopharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgery</td>
<td>Conservation</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>61 (10)</td>
<td>58 (7.2)</td>
</tr>
<tr>
<td>Sex, number</td>
<td>Male</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4</td>
</tr>
<tr>
<td>Stage (%)</td>
<td>I, II or III</td>
<td>27.6%</td>
</tr>
<tr>
<td></td>
<td>IVa or IVb</td>
<td>72.4%</td>
</tr>
</tbody>
</table>

---

### Table 2 Functional scale (QLQ-C30) scores according to surgical vs. conservative treatment. The higher the scope, the better the quality of life.

<table>
<thead>
<tr>
<th>Score: median (SD)</th>
<th>Larynx</th>
<th>Hypopharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgery</td>
<td>Conservation</td>
</tr>
<tr>
<td>General status</td>
<td>66 (25.3)</td>
<td>75 (24.5)</td>
</tr>
<tr>
<td>Physical</td>
<td>87 (16.6)</td>
<td>87 (20.8)</td>
</tr>
<tr>
<td>Role</td>
<td>100 (26.6)</td>
<td>66 (30.1)</td>
</tr>
<tr>
<td>Emotion</td>
<td>75 (24.0)</td>
<td>75 (27.5)</td>
</tr>
<tr>
<td>Cognition</td>
<td>84 (19.7)</td>
<td>100 (24.6)</td>
</tr>
<tr>
<td>Social</td>
<td>84 (32.1)</td>
<td>84 (35.4)</td>
</tr>
</tbody>
</table>
cancer patients in 12 countries [10]: it was shown that the specific section provided information that the generic section could not assess.

The present study identified certain differences in quality of life between patients managed by total (pharyngo-) laryngectomy or with organ conservation. In laryngeal cancer, patients managed by sequential or concurrent radiochemotherapy showed greater symptoms of dry mouth and thick saliva than those undergoing complementary radiation therapy following total laryngectomy, probably due to accumulation of toxicity. Conversely, in hypopharyngeal cancer, patients managed by total pharyngolaryngectomy reported greater difficulties in taste and smell (sensory disorder). These findings show that each type of pharyngolaryngeal cancer treatment impacts different aspects of quality of life.

The literature contains contradictory reports comparing QoL following radiochemotherapy or laryngectomy in laryngeal cancer. The former is associated with significantly better QoL according to Boscolo-Rizzo et al. [11], whereas Hanna et al. [6] found no significant difference. The present results also found no difference between treatment groups on the social aspects of QoL, except for a tendency in hypopharyngeal cancer for "social eating" to be easier following conservative treatment. Physical change and change in self-image, difficulty in communication and social isolation following total laryngectomy may impair quality of life [12], but the present results showed little such impairment, and did not highlight the possible direct relation between physical deficit and social implications. Either patients adapted well to total laryngectomy, or radiochemotherapy induced just as severe deficits and social impact.

More precisely, no difference between treatment groups emerged with respect to voice and swallowing disorder. Clinical experience would have suggested greater differences, with more severe voice disorder associated with laryngectomy and more severe swallowing disorder with radiochemotherapy. Other authors, however, using other QoL assessment tools, reported a similar absence of difference [13,14]. Several factors may explain this. It could testify to the effectiveness of vocal rehabilitation in intensive postoperative speech therapy (esophageal and tracheoesophageal voice training). Secondly, as external radiation therapy was in fact used in both treatment groups, differences in associated complications such as dysphagia
Figure 2  Symptom scale (QLQ-C30, a) and independent item (QLQ-H&N35, b) scores in non-conservative surgical (NC) versus conservative (C) treatment of hypopharyngeal cancer. Boxes represent 25th and 75th percentiles, and median. The lower the score, the better the quality of life. The off-center median indicates the low response homogeneity. Significant difference, \( p < 0.0015 \) (0.05 decision threshold, with Bonferroni correction).

Finally, QoL was assessed at least 1 year after end of treatment, which could have allowed recovery from acute side-effects, whether surgical or medical: treatment-related differences on the various QoL items during the acute phase may have regressed during recovery [15,16].

Finally, the criteria adopted in this QoL questionnaire, and which we considered relevant to our patients' quality of life, may not be the criteria of good quality of life from the point of view of the patients themselves. Physicians and patients probably have different ideas of the latter's quality of life [17]. Other criteria such as depressive syndrome and patients' age and social environment probably also impact quality of life [18].

In the present study, results differed between laryngeal and hypopharyngeal cancer, fairly systematically in favor of conservative treatment in the latter but without systematic difference in the former. One reason may be that surgery for hypopharyngeal carcinoma is more mutilating with respect to the mucosa and muscles, with consequently greater functional sequelae. The proportion of locally more evolved tumors in the surgery group cannot account for the results as a whole, as it was comparable in the two location groups (larynx/hypopharynx). Likewise, age and sex-ratio tended to differ between treatment groups (for both locations), but were generally comparable between the two locations, with a higher proportion of female patients and a lower median age in the conservative treatment group.

The study had several limitations. Analysis was retrospective and compared two non-randomized groups. Certain treatment features could not be controlled, such as: phonatory implantation; unilateral, bilateral, functional or radical lymph-node dissection in the surgery group; or radiation dose, intensity-modulated radiation delivery, and the rhythm and dosage adaptations of the chemotherapy courses. Moreover, the conservative treatment group included different organ-conservation protocols, but sample-size precluded sub-group analysis. Finally, the interval following end of treatment ranged from one to 11 years, constituting a further study limitation.

Conclusion

There was little difference in quality of life between patients with laryngectomy or organ conservation. Quality of life was impaired in all cases, with conservative versus
Quality of life in patients treated for advanced hypopharyngeal or laryngeal cancer

surgical management affecting different aspects. Long-term prospective studies could assess and specify the differences in quality of life associated with these two forms of treatment.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


