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### Abstract

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### Reference

ALLAL, Abdelkarim Said, *et al.* Assessment of quality of life in patients treated with accelerated radiotherapy for laryngeal and hypopharyngeal carcinomas. *Head & Neck*, 2000, vol. 22, no. 3, p. 288-93

DOI : 10.1002/(SICI)1097-0347(200005)22:3<288::AID-HED12>3.0.CO;2-B

PMID : 10748453

Available at:

<http://archive-ouverte.unige.ch/unige:33165>

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# ASSESSMENT OF QUALITY OF LIFE IN PATIENTS TREATED WITH ACCELERATED RADIOTHERAPY FOR LARYNGEAL AND HYPOPHARYNGEAL CARCINOMAS

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Accepted 7 July 1999

**Abstract:** *Background.* This study was conducted to evaluate quality of life (QOL) and functional outcome in patients with carcinomas of the larynx and hypopharynx treated with accelerated radiotherapy (RT).

*Methods.* Between January 1991 and September 1996, 21 patients treated with accelerated concomitant boost RT schedule (69.9 Gy in 5.5 weeks) for laryngeal ( $n = 10$ ) or hypopharyngeal ( $n = 11$ ) carcinomas and who remained free of disease at 1-year minimum follow-up were evaluated. The functional outcome was assessed by the subjective Performance Status Scale for Head and Neck cancer (PSSHN) and general QOL by the European Organization for Research and Treatment of Cancer Core QOL questionnaire (EORTC QLQ-C30). The median length of follow-up was 37 months (range, 13 to 75).

*Results.* The PSSHN scores were 89, 84, and 86, respectively, for eating in public, understandability of speech and normalcy of diet (100 = normal function). Significantly lower scores for understandability of speech were observed in patients with advanced and laryngeal carcinomas. Normalcy of diet was affected negatively by the severity of xerostomia. All mean functional scale scores of the EORTC QLQ-C30 module were 20% to

25% below the higher score. Most of these scale scores were significantly affected by the severity of xerostomia.

*Conclusions.* Patients treated with concomitant boost RT for laryngeal and hypopharyngeal carcinomas appear to have similar QOL and functional outcome to those reported for patients treated with conventional or hyperfractionated RT. As expected, many QOL scales were affected by the severity of xerostomia. © 2000 John Wiley & Sons, Inc. *Head Neck* 22: 288–293, 2000.

**Keywords:** quality of life; accelerated radiotherapy; head and neck cancer

**D**uring the past 2 decades the availability of multimodality approaches has stimulated renewed interest in the preservation of organ function in the treatment of head and neck cancers. Radiation therapy (RT) has been the mainstay of these strategies, either used alone or in combination with surgery or chemotherapy. In addition to the standard oncologic endpoints, quality of life (QOL) has become an important parameter when reporting or comparing results of different treatment strategies. Although the final aim of conservation approaches is to preserve the anatomic integrity of various structures, QOL of the surviving patients may be influenced by addi-

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Presented at the 2nd Annual Meeting of the Scientific Association of Swiss Radiation Oncology, March 20–21, 1998, Lausanne-Switzerland.

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tional factors, including treatment-related side effects and the physiologic function of the preserved organs. In circumstances in which the functional outcome could be expected to have a negative impact on QOL, a radical surgical approach might represent a preferable alternative. Horiot et al<sup>1</sup> documented an increase in severe functional radiation injury in patients treated with accelerated RT compared with those treated with conventional fractionation (14% vs 4%). Although QOL of patients with head and neck cancer has been assessed in several studies after different treatment approaches,<sup>2-5</sup> thus far no reports have been published concerning QOL outcome in patients treated by accelerated RT. Taking into account these considerations, we assessed QOL of patients treated with accelerated RT for laryngohypopharyngeal carcinomas.

At Geneva University Hospital patients with head and neck carcinomas suitable for RT to the primary tumor have been treated since 1991 with a concomitant boost accelerated fractionation schedule. The purpose of this article is to report the impact of this treatment on QOL of patients treated for laryngeal or hypopharyngeal cancers in terms of disease-specific functional and general QOL aspects by use of 1 validated questionnaire for each aspect. The choice of these 2 disease subsites was motivated by their essential role in speech, respiration, and swallowing.

## METHODS AND MATERIALS

**Patient Characteristics.** Between January 1991 and September 1996, 57 patients with carcinomas of the hypopharynx or larynx were treated with accelerated RT. Thirty-one patients were alive at the beginning of this study. Six were excluded from the analysis: 3 had salvage surgery for primary tumor recurrence, 1 was alive with disease, and 2 had less than 1 year's follow-up. The remaining 25 patients were contacted by letter to solicit their cooperation in answering the questionnaires and to arrange an appointment for a clinical examination. One refused to participate in the study while answering that she was feeling well, and 3 did not respond to 2 successive mailings. Thus, 21 of the 25 eligible patients (84%) participated in the study. Patient pretreatment characteristics are given in Table 1. The median follow-up was 37 months (range, 13 to 75).

**Treatment.** The RT schedule has previously been reported.<sup>6</sup> The schedule planned to deliver a total dose of 69.9 Gy in 41 fractions over a period of 38

**Table 1.** Initial patient characteristics.

Characteristics	No. patients
Median age, yr (range)	63.5 (40-78)
Gender: male/female	17/4
WHO performance status	
0	15
1 and 2	6
Location	
Larynx	10
Hypopharynx	11
TNM classification (UICC 1987)	
T1-2	11
T3-4	10
N0/N1	10/3
N2/N3	7/1
AJCC stage	
I/II	3/2
III/IV	6/10

days, by use of megavoltage beams. Involved sites and areas of potential microscopic disease (generally both sides of the neck down to the clavicles) received 50.4 Gy in 28 fractions over 5.5 weeks, and the boost to initial involved sites delivered 19.5 Gy in 13 fractions of 1.5 Gy given as a second daily fraction in a progressively accelerated fashion. The minimum interval between the 2 daily fractions was 6 hours. Before RT, 6 patients had a unilateral radical neck dissection, including a contralateral modified neck dissection in 1 patient. No patients had surgery to the primary tumor. Six patients received chemotherapy concomitantly with RT, either alone ( $n = 3$ ) or with neoadjuvant and/or adjuvant chemotherapy ( $n = 3$ ). All patients received cisplatin (CDDP, 100 mg/m<sup>2</sup>)-based chemotherapy, associated with 5-fluorouracil (5-FU, 1000 mg/m<sup>2</sup> daily for 5 days) in 5 patients. Three patients received 3 cycles and 3 received 2 cycles.

**QOL Assessment.** The assessment of QOL was performed by use of two distinct questionnaires, 1 for disease-specific measures and 1 for general QOL measures, chosen for their proven validity and reliability: the Performance Status Scale for Head and Neck cancer (PSSHN) developed by List et al<sup>3</sup> and the European Organization for Research and Treatment of Cancer Core QOL questionnaire (EORTC QLQ-C30).<sup>7</sup>

**PSSHN.** This questionnaire is designed to assess head and neck area dysfunction. It is a clinician-rated tool consisting of 3 subscales assessing eating in public, understandability of speech, and

normalcy of diet. The 3 subscales are rated from 0 to 100, with 100 representing normal function.

**EORTC QLQ-C30.** This is a patient self-rating questionnaire that comprises 6 multi-item function scales measuring physical, role, social, emotional, and cognitive functions and overall QOL. Separate symptom scales are included to assess pain, fatigue, and emesis, and 5 single items to measure bowel function, breathing, appetite, and sleeping disturbances. A final item evaluates the economic consequences of the disease. All measurements are linearly transformed such that all scales range from 0 to 100, with higher scale scores representing a higher level of functioning for the 6 function multi-items and a higher level of symptoms/problems for the symptom/economic items.

**Statistical Methods.** The unpaired *t* test was used to assess for significant differences between score means obtained in groups defined using certain selected factors (see later). All factors studied were selected to define groups of at least 10 patients except for xerostomia factor. The groups are defined as follows: age,  $\leq 63.5$  years vs  $>63.5$  years; tumor location, hypopharynx versus larynx; tumor stage, T1-2 vs T3-4; treatment strategies, RT alone (10 patients) vs RT and neck dissection and/or chemotherapy (11 patients); length of follow-up,  $\leq 37$  months versus  $>37$  months; xerostomia,  $\leq$  grade 1 (13 patients) versus  $>$  grade 1 (8 patients).

## RESULTS

**PSSHN Scores.** For all patients, the PSSHN scores were 89 (SD, 18), 84 (SD, 20), and 86 (SD, 18), respectively, for eating in public, understandability of speech, and normalcy of diet. For the eating in public subscale no significant difference was found in subgroups of patients according to the factors tested. For the understandability of speech subscale, significantly lower scores were reported by patients with laryngeal carcinoma ( $p = .03$ ) or with advanced primary tumors ( $p = .03$ ). The score for the normalcy of diet subscale was not significantly different in subgroups, although a trend to a lower score was observed in patients with grade 2 or 3 (RTOG) xerostomia ( $p = .08$ ). None of the function scores improved significantly with longer follow-up, but a trend to improvement with time was found in the normalcy of diet score ( $p = .06$ ).

**EORTC QLQ-C30 Scores.** The mean scores for all patients are given in Table 2. Patients with high-grade xerostomia had significantly lower score means for physical function ( $p = .01$ ), role function ( $p = .001$ ), emotional function ( $p = .05$ ), social function ( $p = .05$ ), and overall QOL ( $p = .002$ ). For the cognitive function score, no significant differences were observed according to the factors tested. The social function score was significantly lower for patients with T3-4 tumors ( $p = .049$ ). Besides the clear dependence on the degree of xerostomia, the overall QOL score was not significantly correlated with the other factors. All functional scale scores were at least slightly improved for follow-up times exceeding the median values, but none achieved significance.

In the fatigue symptom scale, significantly higher scores were reported by patients with advanced age ( $p = .03$ ). Also patients with severe xerostomia ( $p = .06$ ) tended to have higher scores for this symptom, whereas the length of follow-up appeared to have no impact. For the pain symptom scale, a markedly higher score was observed in patients having nodal involvement ( $p = .11$ ). Dyspnea symptom score was significantly higher in patients with T3-4 tumors ( $p = .05$ ), those with advanced age ( $p = .04$ ), and those having severe

**Table 2.** EORTC QLQ-C30 mean scale and single items scores for the Geneva University Hospital (GUH) and the Norwegian Radium Hospital (NRH, ref. 4) series.

	Concomitant boost RT larynx and hypopharynx GUH series, <i>n</i> = 21	Conventional RT H&N (50% larynx) NRH series, <i>n</i> = 103
Functional scales		
Physical function	75 (23)	74
Role function	76 (34)	72
Emotional function	76 (29)	77
Cognitive function	81 (21)	80
Social function	84 (22)	73
Global quality of life	73 (20)	61
Symptom scales		
Fatigue	33 (32)	32
Pain	17 (29)	19
Nausea and vomiting	8 (16)	6
Single items		
Dyspnea	28 (34)	20
Sleep disturbance	16 (29)	22
Appetite loss	24 (35)	12
Diarrhea	6 (22)	14
Constipation	14 (22)	17
Financial impact	5 (12)	19

Abbreviations: H&N, head and neck; RT, radiation therapy.

xerostomia ( $p = .02$ ), with no apparent change with length of follow-up. Appetite loss score was significantly higher in patients with high-grade xerostomia ( $p = .02$ ). The nausea-vomiting symptom score was significantly higher in patients with high-grade xerostomia ( $p = .01$ ), although this symptom decreased significantly in patients with long follow-up ( $p = .03$ ).

## DISCUSSION

The choice of treatment regimen can have profound implications for the QOL of patients surviving head and neck cancer because therapy can result in alterations of some of the most fundamental functions, including those of communication, nutrition, and respiration.<sup>8,9</sup> A small number of studies have addressed QOL issues in head and neck cancers, either prospectively<sup>10,11</sup> or, more often, retrospectively in patients submitted to different treatment approaches.<sup>3-5,12</sup> Although treatment results and complications have been reported in patients treated with modified fractionation schedules, little is known about QOL after such more aggressive treatment programs. Recently, in an EORTC randomized trial, Horiot et al<sup>1</sup> documented an increase in severe functional radiation injury in patients treated with accelerated RT compared with those treated with conventional fractionation (14% vs 4%). This observation led the authors to caution against the subsequent use of this particular accelerated regimen despite its superiority in terms of locoregional control. With these results in mind, we assessed QOL of patients treated with concomitant boost accelerated RT for laryngohypopharyngeal carcinomas. For this purpose 2 questionnaires were used, 1 for disease-specific parameters (PSSNH) and 1 for general QOL measurements (EORTC QLQ-C30); they were chosen for their proven validity and reliability. Whereas the EORTC QLQ-C30 is a patient self-rating module, the PSSNH is clinician-administered, with the disadvantage that the potential influence of the clinician on responses cannot be completely eliminated. Nonetheless, we retained this module because of the large experience with its use in head and neck cancer patients and the available data that made possible the comparison of our data with those of others.

In this series the results obtained by use of the PSSNH module appear rather satisfactory, taking into consideration the relatively advanced disease stage, the aggressiveness of the RT schedule, and the structures included in the high-dose vol-

ume. Few previous publications have addressed QOL in patients with laryngohypopharyngeal carcinomas. Moreover, differences in patients' characteristics have made difficult any direct comparisons. In 7 patients with early stage laryngeal carcinoma, evaluated 6 months after conventional RT, List et al<sup>11</sup> reported a median value of 100 for the 3 PSSHN subscales. Our median value in the 11 patients with T1-2 tumors was also 100, although the overall mean values were inferior, probably because of inclusion of patients with advanced neck disease. Compared with the results reported by Long et al<sup>4</sup> in a series of 50 patients treated at Loma Linda University by radical surgery with or without RT, our results are superior for the 3 PSSHN subscales (Table 3). However, this latter series included cancers arising in different head and neck regions (44% larynx), recurrent disease, and patients with progressive disease after RT.

On the other hand, our results compare favorably with those obtained after treatment using other unconventional treatment programs. List et al<sup>13</sup> in a series of 34 patients treated with concurrent bifractionated RT and multidrug chemotherapy (5-fluorouracil, hydroxyurea, and cisplatin) showed poor PSSHN scores because 61% of patients had feeding tubes and 88% were unable to take solid food 6 months after the end of treatment.

Despite certain weaknesses that are inherent to the cross-sectional design of this study and to the small number of patients included, we tried to identify factors associated with lower QOL scores. The results suggest a possible association with certain clinical factors that merit investigation in future large prospective studies. For the PSSHN eating in public subscale, although not signifi-

**Table 3.** PSSHN function, mean scores for Geneva University Hospital (GUH), and for Loma Linda University (LLU, ref. 4).

	GUH larynx and hypopharynx accelerated RT (SD) <i>n</i> = 21	LLU H&N (44% larynx) surgery (SD) <i>n</i> = 50
Eating in public	89 (18)	71 (35)
Understandability of speech	84 (20)	71 (31)
Normalcy of diet	86 (18)	69 (35)

Abbreviations: H&N, Head and neck; SD, standard deviations.

cant, lower scores were observed in patients with hypopharyngeal carcinomas that may have been a reflection of the multimodal therapy and the extended RT fields more often used in these patients. As expected, the normalcy of diet subscale tended to be influenced by the severity of xerostomia, with a trend toward a significant improvement with time. The latter might result from the slight recovery of the salivary flow or patient accommodation to the xerostomia with time. For the understandability of speech, patients with laryngeal tumors and advanced disease showed significantly lower scores that did not improve with longer follow-up. This may be explained by the irreversible destruction of laryngeal structures involved by laryngeal tumors or in bulky disease presentations.

Although a longitudinal study comparing both pretreatment and posttreatment assessments would be preferable, our data using the EORTC QLQ-C30 questionnaire may give input to prospective hypotheses testing. Thus, the results obtained seem to be equivalent to those obtained by Bjordal et al<sup>2</sup> in 103 patients treated with conventionally fractionated RT for various head and neck cancers (50% larynx) (Table 2). Although differences in patients' characteristics may prevent any adequate comparison, social and global QOL scores were higher in our series (possibly because of differences in social habits and perception of disease impact), whereas dyspnea and appetite loss symptoms were reported more often by our patients.

In this series, most of EORTC QLQ-C30 parameters were significantly influenced by the severity of xerostomia. The possible preponderant impact of xerostomia on QOL is not surprising, considering its negative influence on patient comfort and its role in promoting different problems, such as dental decay, loss of mandibular integrity, and candidosis. As expected, patients with advanced age reported lower scores for several functions (physical, role, emotional, cognitive, social) and adverse symptoms (fatigue, dyspnea, and appetite loss). All these findings were not fully related to the treatment received but rather to the conjunction of various other medical and social problems. Finally, patients with advanced disease or hypopharyngeal carcinomas seemed to have lower function scores and higher symptom scores.

In conclusion, QOL and functional outcome in our patients treated conservatively with concomi-

tant boost RT for laryngeal and hypopharyngeal carcinomas appear to be similar to those obtained in patients treated with conventional or hyperfractionated RT, although these findings need to be confirmed in a prospective randomized trial. By assessing the impact of different clinical and therapeutic factors, some relevant findings are provided that may serve as hypotheses to be tested prospectively. Considering the impact of xerostomia on most scales studied, special attention should be paid during treatment planning in an attempt to limit salivary gland irradiation as much as clinically permissible. In addition, the timely use of pilocarpine to stimulate salivary flow could be envisioned. When assessing the functional and the QOL outcome for head and neck cancer patients, it appears necessary to use both disease-specific and general QOL questionnaires because many items are complementary. Clearly the use of a single module is inadequate for assessing all QOL aspects.

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