



Quality of life after surgical treatment for tongue cancer

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Background: The aim of this study is to evaluate the quality-of-life (QoL) among patients who underwent surgical treatment for squamous carcinoma of the oral tongue at the 12 de Octubre Hospital, Madrid, Spain.

Methods: QoL of patients suffering from tongue cancer was evaluated using patients' response to the Spanish version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and Head and neck cancer-35 (QLQ-H&N35). Sixty patients were included in a cross-sectional observational study. These patients were in line with the inclusion criteria submitted and were surgically treated between 2004 and 2014. They were classified according to sex, age, disease stage and whether or not they had received radiotherapy (RT) treatment.

Results: Global EORTC QLQ-C30, social functioning, QoL scale and role scores for different stages showed significant differences ($P=0.041$). QLQ-H&N35 questionnaires also found differences for swallowing, senses, speech, social eating, and social contact. Radiated patients had a significantly greater impairment in all symptoms at the EORTC QLQ-H&N35 scales. Dental problems ($P=0.028$), trismus ($P<0.001$) and sticky saliva ($P=0.021$) were also frequent in these patients. No significant results were found for age groups. Women scored higher than men for pain, dry mouth, sticky saliva and fatigue.

Conclusions: Questionnaires such as H&N35 and QLQ-C30 serve as vital instruments in quantitatively measuring QoL. Adjuvant RT and advanced disease stage were shown to negatively affect QoL scores. No differences for age were found, whereas higher scores for pain, dry mouth, sticky saliva and fatigue were found for women compared to men.

Keywords: Quality-of-life (QoL); tongue cancer; head and neck cancer (HNC); European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30); European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and neck cancer-35 (EORTC QLQ-H&N35)

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Introduction

Head and neck cancer (HNC) constitutes approximately 5% of the total number of malignant tumors worldwide. Of these, Squamous cell carcinoma is considered the most common histological subtype, comprising almost 90% of all known cases (1).

According to the Spanish Network of Cancer Registries (REDECAN) database, oral and oropharyngeal cancer is the seventh most frequent cancer in Spain, with 8,486 new cases in 2019. The estimated incidence rate for oral and oropharyngeal cancer in the European standard population is 18.0 per 100,000 person-years (2). Moreover, the interactive epidemiological information server (ARIADNA), the Ministry of Science and Innovation of the Government of Spain and the Carlos III Health Institute published that the mortality rate for men has decreased to 5.9 since 1975. Meanwhile this rate has increased to 1.46 in women (3).

Survival has traditionally been the main, and sometimes only, parameter to assess the success of treatment in patients with HNC. However, quality-of-life (QoL) has recently taken a leading role as a determining factor in this regard. Thus, increasing its presence in recent scientific publications. In fact, some authors suggest that QoL may be a prognostic value if evaluated before treatment (4-6).

Patients with HNC not only have to cope with a life-threatening disease, but also with the severe impact of the tumor and its treatments in their daily life. This is especially important because of both functional and aesthetic implications, often not sufficiently considered by clinicians.

Through the use of QoL surveys, the patient outlines which aspects of the disease he/she considers most incapacitating, thus participating in therapeutic decisions (4-6).

Since the mid-twentieth century, surgery has been the backbone for treatment of oral cancer. Classically, patients with local tumors [stages I and II of the TNM classification according to the American Joint Committee on Cancer (AJCC)] (7) are considered to have a positive prognosis after undergoing surgery or radiotherapy (RT). However, patients with locally advanced tumors or with cervical lymph node extension (stages III and IV of the AJCC) have much lower survival rates and require multimodal treatments. In these patients, survival rates have not undergone dramatic improvements over the last few decades, however QoL has significantly improved as a result of the introduction of new, more selective forms of RT, chemoradiotherapy (RT-QT), molecular therapy, and microsurgical transplantation techniques to reconstruct

complex oro-mandibular defects (8).

In order to assess this multidimensional and subjective concept, different methods and models have emerged. Early models including semi-structured interviews have since been discarded due to their great time consumption. Currently the most commonly used method consists of self-assessment questionnaires completed by the patient.

The models selected for this study are those proposed by the European Organization for Research and Treatment of Cancer (EORTC) (9,10). This is due to the fact that they encompass a large number of items and have been translated and validated for use in Spain. These questionnaires include a general survey [Quality of Life Questionnaire Core 30 (QLQ-C30)] and a specific assessment for Head & Neck Cancer [Quality of Life Questionnaire Head and Neck Cancer-35 (QLQ-H&N35)] (6).

The objective of this study is to determine QoL in a sample of patients diagnosed with oral tongue squamous cell carcinoma undergoing surgery at the 12 de Octubre Hospital using both the EORTC QLQ-C30 and QLQ-H&N35 questionnaires. Our null hypothesis was the absence of effect of demographic characteristics and treatment protocols in QoL. We present the following article in accordance with the STROBE reporting checklist (available at <https://fomm.amegroups.com/article/view/10.21037/fomm-21-97/rc>).

Methods

The design used for this study was a cross-sectional observation. The target population included patients with tongue cancer undergoing surgical treatment at the Oral and Maxillofacial Surgery Department, 12 de Octubre Hospital (Madrid, Spain) between 2004 and 2014.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics committee of the 12 de Octubre Hospital (No. 21/246) and informed consents were obtained from patients.

The inclusion criteria were as follows: patients over 18 years of age, able to read and understand the questionnaires on their own and willing to participate in the study; histopathological diagnosis of squamous cell carcinoma of the oral tongue; treated between 2004 and 2014 (inclusive) either by surgery or with adjuvant treatment after resection (RT, Combined chemotherapy and RT, or RT combined with molecular therapy). Standard surgical management included glossectomy, elective or therapeutic neck dissection and free

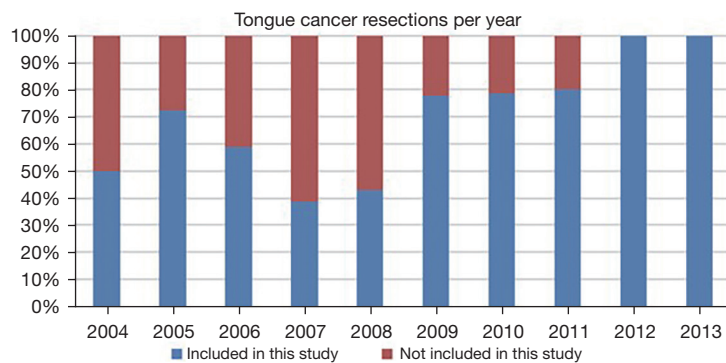


Figure 1 Number of Glossectomies per year. This graph shows the relative percentage of glossectomies performed each year that were included in the study.

flap reconstruction for resections greater than 1/3 of the mobile tongue (or significantly affecting tongue mobility).

The exclusion criteria were as follows: patients with palliative treatment or those with comorbidities or mental disabilities that prevented the completion of the questionnaires.

The patients selected to participate in the study were extracted from our own surgical database and registry, which included all surgical interventions performed for lingual carcinomas. All patients were treated by the Oncology and Reconstructive Team at the Maxillofacial Surgery Department in our institution. This group includes six permanent faculty members.

From a total of 154 patients at the database, 48 were deceased (31.17%), 22 could not be reached by telephone (14.29%), 12 rejected participation (7.79%) and 12 had physical and/or psychic disabilities that invalidated their inclusion (7.79%). A total of 60 patients (38.96%) were eligible and finally included for the study. Group distribution was carried out following the age groups proposed by the EORTC (<40, 40–49, 50–59, 60–69, 70–80, ≥80) (9).

During 2014, patients in our cohort were approached by a staff member of our department at the outpatient clinic. Study objectives, characteristics, data confidentiality and voluntary nature were explained and informed consents were signed after patient acceptance. Afterward, surveys were completed without supervision in order to avoid any bias. Nevertheless, a small group of patients filled-out and sent the questionnaires by mail. Due to the impossibility of physical travel to the hospital.

Patients completed the Spanish version of the EORTC QoL questionnaires (QLQ-C30 version 3.0 and QLQ-H&N35) at least 6 months after surgery. The survey scores were analyzed following the EORTC Scoring Manual

guidelines (10) (3rd edition). As per these guidelines, the results obtained from the questionnaires were transformed to a score from 0 to 100. High scores on the functional spheres and global health status (GHS) scales reflect a greater level of the assessed activities, while high scores on the symptom scales and individual items denote greater symptoms and problems.

Statistical analysis

The data was analyzed using the SPSS version 22.0.0. statistical program. A normality test using the Shapiro-Wilk test (for $n < 30$) showed a non-normal distribution of the variables studied. Thus, non-parametric tests were applied in contrasting hypotheses. As a result, for comparisons between two groups, a Mann-Whitney test was applied, choosing as significant values $P < 0.05$. For comparisons greater than two groups, Kruskal-Wallis test was employed, establishing values of $P < 0.05$ divided by the number of groups considered as statistically significant (Bonferroni correction).

Results

A total of 60 patients were included, all surgically treated from 2004–2014. The Spanish version of the EORTC QoL questionnaires (QLQ-C30 version 3.0 and QLQ-H&N35) was completed at least 6 months after surgery. Moreover, sampling time after surgery ranged from 6 to 134 months (median = 54 months) and the number of patients that underwent surgery each year is described in *Figure 1*.

The mean age was 66.85 ± 13.93 years [standard deviation (SD)]. 40 were women and 20 were men. The patients were divided into three groups depending on whether their disease was staged as local (67.80%), advanced (13.56%)

Table 1 Survival rates (n=137)

	3-year follow-up	5-year follow-up	8-year follow-up
Survival rate	0.73	0.66	0.61
Deaths caused by cancer	0.24	0.29	0.27

Table 2 Comparison of QoL according to the sex (EORTC QLQ-C30)

Comparison of QoL according to the sex (EORTC QLQ-C30)	Median (P25–P75)		P value	Median (P25–P75), total sample (n=60)
	Male (n=20)	Female (n=40)		
Functional scales				
Physical functioning	100.00 (90–100.00)	86.67 (73.33–100.00)	0.055	93.33 (76.67–100.00)
Role	100.00 (66.67–100.00)	100.00 (66.67–100.00)	0.844	100 (66.67–100.00)
Emotional functioning	91.67 (66.67–100.00)	75 (58.33–83.33)	0.068	75.00 (58.33–91.67)
Cognitive functioning	83.33 (83.33–100.00)	91.67 (66.67–100.00)	0.469	83.33 (83.33–100.00)
Social functioning	100.00 (66.67–100)	100.00 (75–100)	0.862	100.00 (66.67–100)
GHS	70.83 (54.17–87.50)	66.67 (50–83.33)	0.419	66.67 (50–83.33)
Symptom scale				
Fatigue	0 (0–33.33)	22.22 (11.11–44.44)	0.042	16.67 (0–33.33)
Nausea y vomiting	0 (0–0)	0 (0–0)	0.243	0 (0–0)
Pain	8.33 (0–33.33)	33.33 (0–50)	0.146	16.67 (0–50)
Individual items				
Dyspnoea	0 (0–16.67)	0 (0–33.33)	0.385	0 (0–33.33)
Loss of appetite	0 (0–33.33)	0 (0–33.33)	0.365	0 (0–33.33)
Insomnia	0 (0–0)	0 (0–0)	0.663	0 (0–0)
Constipation	0 (0–33.33)	33.33 (0–66.67)	0.120	0 (0–33.33)
Diarrhoea	0 (0–0)	0 (0–0)	0.658	0 (0–0)
Economic impact	0 (0–33.33)	0 (0–33.33)	0.872	0 (0–33.33)

Mann-Whitney U test was used to assess differences. QoL, quality-of-life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS, global health status.

or metastatic-recurrent (18.64%). 19 patients received postoperative adjuvant RT (31.67%). The results of the scales and individual items of the questionnaires were compared according to age, sex, tumor stage and treatment or not with postoperative RT. In addition, survival follow-up was carried out at 3 separate stages for 137 patients of the original 154 included in the database.

Survival

Table 1 reflects survival rates of 137 patients included in this

study at 3 stages of post-operative follow-up: 3-, 5-, and 8-year follow-up. At 3-year follow-up, survival rate stood at 76%, dropping to 66% at 5-year interval, and finalizing at 61% at the 8-year cut-off. In addition, tongue cancer was responsible for 24%, 29%, and 27% of all deaths at each respective stage.

QoL comparison in relation to sex

Table 2 compares QLQ-C30 data according to sex. High scores were found in all five functional scales. While scores

Table 3 Comparison of QoL according to the sex (EORTC QLQ-H&N35)

Comparison of QoL according to the sex (EORTC QLQ-H&N35)	Median (P25–P75)		P value	Median (P25–P75), total sample (n=60)
	Male (n=20)	Female (n=40)		
Functional scales				
Pain	12.50 (0–20.83)	16.67 (8.33–45.83)	0.037	16.67 (8.33–37.50)
Swallowing	8.33 (0–20.83)	8.33 (0–25.00)	0.818	8.33 (0–25.00)
Senses (taste and smell)	0 (0–16.67)	16.67 (0–33.33)	0.091	0 (0–33.33)
Speech	11.11 (0–22.22)	11.11 (0–33.33)	0.442	11.11 (0–33.33)
Eating in public	8.33 (0–29.17)	12.50 (0–41.67)	0.365	12.5 (0–37.50)
Social contact	0 (0–13.33)	0 (0–20.00)	0.592	0 (0–20.00)
Sexuality	33.33 (0–66.67)	0 (0–33.33)	0.267	0 (0–66.67)
Individual items				
Dental problems	0 (0–66.67)	33.33 (0–66.67)	0.193	33.33 (0–66.67)
Trismus	0 (0–33.33)	0 (0–33.33)	0.628	0 (0–33.33)
Dry mouth	0 (0–66.67)	66.67 (33.33–66.67)	0.044	66.67 (0–66.67)
Sticky saliva	0 (0–33.33)	33.33 (0–66.67)	0.034	33.33 (0–66.67)
Cough	33.33 (0–33.33)	0 (0–33.33)	0.065	0 (0–33.33)
General malaise	0 (0–33.33)	0 (0–33.33)	0.862	0 (0–33.33)
Pain medication	0 (0–100.00)	0 (0–100.00)	0.856	100.00 (0–100.00)
Nutritional supplements	0 (0–50.00)	0 (0–0)	0.447	100.00 (100.00–100.00)
Feeding tube	0 (0–0)	0 (0–0)	0.999	100.00 (100.00–100.00)
Weight loss	0 (0–0)	0 (0–0)	0.826	100.00 (100.00–100.00)
Weight gain	0 (0–50.00)	0 (0–100.00)	0.436	100.00 (0–100.00)

Mann-Whitney U test was used to assess differences. QoL, quality-of-life; EORTC QLQ-H&N35, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and neck cancer-35.

for symptom scales and individual items were low. As for GHS, a median of 66.67 was obtained.

No significant differences in GHS score were observed with respect to sex. Regarding symptoms, statistically significant higher scores were observed in women for fatigue.

In the specific module H&N35 (Table 3), the items most frequently altered were those related to xerostomia, dental problems, pain and disfunction in taste and smell. Significant differences with respect to sex were observed for pain, dry mouth, and sticky saliva.

QoL comparison in relation to age

Regarding age groups, no significant differences were

observed (Tables 4, 5) in any of the questionnaires.

QoL comparison in relation to tumoral stage

As for tumoral stages (Table 6), the QLQ-C30 showed higher scores both for GHS and in social functioning when patients were treated for local tumors versus locally advanced or metastatic-recurrent. Differences between stages for fatigue and pain were observed, although not statistically significant.

The H&N35 module revealed statistically significant differences in scores referring to the functional scales for speech, swallowing, eating in public, senses, and social contact. There were also differences, although not statistically significant, in items such as trismus and xerostomia.

Table 4 Comparison of QoL in relation to age (EORTC QLQ-C30)

Comparison of QoL in relation to age (EORTC QLQ-C30)	Median (P25–P75)					P value	
	Age <40 years (n=2)	Age 40–49 years (n=5)	Age 50–59 years (n=14)	Age 60–69 years (n=13)	Age 70–79 years (n=15)		Age ≥80 years (n=11)
Functional scales							
Physical functioning	96.67 (93.33–100.00)	93.33 (93.33–100.00)	96.67 (86.67–100.00)	93.33 (86.67–100.00)	80.00 (73.33–100.00)	86.67 (40.00–100.00)	0.545
Role	83.33 (66.67–100.00)	100.00 (66.67–100.00)	100.00 (66.67–100.00)	100.00 (66.67–100.00)	100.00 (83.33–100.00)	100.00 (33.33–100.00)	0.994
Emotional functioning	87.50 (75.00–100)	66.67(58.33–66.67)	75.00 (75.00–91.67)	66.67.00 (37.50–100.00)	75.00 (41.67–91.67)	83.33 (63.67–100.00)	0.663
Cognitive functioning	83.33 (66.67–100)	83.33 (83.33–100)	91.67 (83.33–100)	100 (83.33–100)	100 (83.33–100)	83.33 (66.67–83.33)	0.329
Social functioning	58.33 (33.33–83.33)	66.67 (66.67–100.00)	100.00 (100.00–100.00)	100.00 (83.33–100.00)	100.00 (66.67–100.00)	100.00 (83.33–100.00)	0.290
GHS	70.83 (58.33–83.33)	83.33 (50.00–100.00)	66.67 (33.33–83.33)	83.33 (66.67–91.67)	62.50 (50.00–83.33)	66.67(41.67–75)	0.586
Symptom scale							
Fatigue	16.67 (0–33.33)	33.33 (0–33.33)	11.11 (0–33.33)	11.11 (11.11–33.33)	22.22 (11.11–44.44)	33.33 (0–55.56)	0.937
Nausea y vomiting	8.33 (0–16.67)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.294
Pain	33.33 (33.33–33.33)	33.33 (0–33.33)	16.67 (0–66.67)	16.67 (0–50.00)	16.67 (0–50.00)	33.33 (0–50.00)	0.988
Individual items							
Dyspnoea	16.67(0–33.33)	0 (0–0)	0 (0–33.33)	0 (0–33.33)	0 (0–33.33)	0 (0–0)	0.901
Loss of appetite	66.67 (33.33–100.00)	16.67 (0–50.00)	0 (0–33.33)	0 (0–33.33)	0 (0–33.33)	0 (0–100)	0.466
Insomnia	0(0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–33.33)	0 (0–33.33)	0.877
Constipation	0(0–0)	0 (0–0)	0 (0–33.33)	0 (0–50.00)	66.67 (0–100)	33.33 (0–33.33)	0.740
Diarrhoea	0(0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–33.33)	0.126
Economic impact	16.67 (0–33.33)	0 (0–33.33)	16.67 (0–33.33)	0 (0–0)	0 (0–0)	0 (0–0)	0.522

Kruskal-Wallis test was used to assess differences. QoL, quality-of-life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS, global health status.

Table 5 Comparison of QoL in relation to age (EORTC QLQ-H&N35)

Comparison of QoL in relation to age (EORTC QLQ-H&N35)	Median (P25-P75)					P value	
	Age <40 years (n=2)	Age 40-49 years (n=5)	Age 50-59 years (n=14)	Age 60-69 years (n=13)	Age 70-79 years (n=15)		Age ≥80 years (n=11)
Functional scales							
Pain	25.00 (8.33-41.67)	16.67 (8.33-16.67)	16.67 (0-41.67)	16.67 (8.33-33.33)	16.67 (16.67-50.00)	8.33 (0-41.67)	0.882
Swallowing	8.33 (0-16.67)	0 (0-8.33)	12.50 (0-25.00)	0 (0-8.33)	8.33 (0-41.67)	0 (0-25.00)	0.584
Senses (taste and smell)	8.33 (0-16.67)	16.67 (0-66.67)	16.67 (0-33.33)	0 (0-16.67)	16.67 (0-50.00)	0 (0-33.33)	0.445
Speech	16.67 (0-33.33)	11.11 (11.11-33.33)	5.56 (0-22.22)	22.22 (11.11-33.33)	22.22 (0-44.44)	0 (0-22.22)	0.334
Eating in public	25.00 (0-50.00)	33.33 (8.33-50.00)	8.33 (0-33.33)	16.67 (0-25.00)	16.67 (0-58.33)	0 (0-41.67)	0.635
Social contact	10 (6.67-13.33)	0 (0-26.67)	0 (0-6.67)	6.67 (0-20.00)	6.67 (0-26.67)	0 (0-20.00)	0.703
Sexuality	0 (0-0)	16.67 (0-33.33)	0 (0-66.67)	33.33 (0-66.67)	0 (0-83.33)	0 (0-50.00)	0.792
Individual items							
Dental problems	16.67 (0-33.33)	33.33 (0-33.33)	33.33 (33.33-66.67)	33.33 (0-100.00)	33.33 (0-100.00)	33.33 (0-66.67)	0.879
Trismus	33.33 (33.33-33.33)	33.33 (0-33.33)	0 (0-66.67)	33.33 (0-33.33)	0 (0-0)	0 (0-0)	0.101
Dry mouth	33.33 (0-66.67)	33.33 (0-33.33)	66.67 (0-66.67)	50.00 (33.33-83.33)	66.67 (33.33-100.00)	33.33 (0-66.67)	0.421
Sticky saliva	50.00 (33.33-66.67)	33.33 (33.33-33.33)	33.33 (0-66.67)	33.33 (0-66.67)	33.33 (0-100.00)	0 (0-33.33)	0.538
Cough	16.67 (0-33.33)	0 (0-33.33)	0 (0-33.33)	33.33 (0-33.33)	16.67 (0-66.67)	0 (0-33.33)	0.570
General malaise	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-33.33)	0 (0-33.33)	33.33 (0-66.67)	0.226
Pain medication	50.00 (0-100.00)	0 (0-100.00)	0 (0-100.00)	0 (0-100.00)	0 (0-100.00)	100.00 (100.00-100.00)	0.239
Nutritional supplements	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-100.00)	0 (0-0)	0 (0-0)	0.783
Feeding tube	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	1.000
Weight loss	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-100.00)	0 (0-100.00)	0.349
Weight gain	0 (0-0)	0 (0-0)	0 (0-100.00)	0 (0-100.00)	0 (0-100.00)	0 (0-100.00)	0.891

Kruskal-Wallis test was used to assess differences. QoL, quality-of-life; EORTC QLQ-H&N35, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and neck cancer-35.

Table 6 Impact of tumor stage on QoL

Impact of tumor stage on QoL	Median (P25–P75)			P value
	Local (n=41)	Locally advanced (n=8)	Metastatic/recurrent (n=11)	
EORTC QLQ-C30				
Functional scales				
Role	100.00 (83.33–100.00)	66.67 (25–91.67)	91.67 (50.00–100.00)	0.032
Social functioning	100.00 (100.00–100.00)	91.67 (66.67–100.00)	66.67 (66.67–100.00)	0.012
GHS	75.00 (54.17–83.33)	70.83 (58.33–100.00)	50.00 (41.67–66.67)	0.041
EORTC QLQ-H&N35				
Swallowing	0 (0–41.67)	20.83 (0–50.00)	33.33 (8.33–66.67)	<0.001
Senses (taste and smell)	0 (0–100.00)	25.00 (0–100.00)	33.33 (0–66.67)	0.042
Speech	5.56 (0–77.78)	11.11 (0–66.67)	33.33 (0–66.67)	0.019
Eating in public	0 (0–50.00)	33.33 (0–100.00)	33.33 (16.67–100.00)	<0.001
Social contact	0 (0–73.33)	6.67 (0–60.00)	20.00 (0–73.33)	0.009

Kruskal-Wallis test was used to assess differences. QoL, quality-of-life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS, global health status; EORTC QLQ-H&N35, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and neck cancer-35.

QoL comparison in relation to adjuvant therapy

Patients who received adjuvant RT (Table 7) showed statistically significant differences in all the H&N35 scales as well as in the following items: trismus, sticky saliva, and dental problems. As for the QLQ-C30 module, statistically significant results were found for social functioning, fatigue, dyspnea and insomnia. Results were statistically inconclusive for the GHS.

Discussion

QoL was initially studied in oncological patients in the 1970s. It was first included as a keyword by the United States National Library of Medicine MEDLINE in 1977 (11). Since then, it has remained a fundamental topic in cancer research, especially in Head and Neck cancer (12,13).

Many scores have been used in order to assess QoL in Head and Neck cancer. During our study, EORTC QLC-C30 and QLQ-H&N35 questionnaires were used. Nevertheless, QLQ-H&N43 was released in 2015 (14) a few months after our sampling was conducted, with it now considered a superior module to the ones used in this study.

In fact, Arraras *et al.* (15) studied the QoL outcomes in Head and Neck cancers and concluded that Oral and Oropharynx cancers have the worst outcomes regarding

QoL. Our results show an acceptable overall QoL with low symptoms (Global Health Status of QoL 66, 67/100).

The majority of the published cohorts include patients with a higher percentage of male patients and smoking habits (16). Nevertheless, our data found a higher female ratio (40:20). Moreover, our initial cohort also included 73 males (47.41%) and 81 females (52.59%), displaying a higher number of female survivors for tongue cancer in our area (17).

As far as age is concerned, our study showed a high incidence in elderly patients (43.33% of our cohort were over 70 years old). This is probably due to the inverted population pyramid and longer life expectancy in our country and the South Madrid area.

Finally, our survival rate is similar to other developed countries. For instance, van Dijk *et al.* (18) published a 5-year survival of 62% between 2006–2010 in Netherlands and the SEER cancer statistics review reported a 5-year survival of 65.8% for patients treated for oral tongue cancer from 2008–2014 (19).

Stage of disease

Tongue cancer is one of the most benign forms of oral cancer. Our survival and disease-specific survival rates

Table 7 Impact of radiotherapy on QoL

Impact of radiotherapy on QoL	Median (P25–P75)		P value
	No radiotherapy (n=41)	Radiotherapy (n=19)	
EORTC QLQ-C30			
Functional scales			
Social functioning	100.00 (100.00–100.00)	83.33 (66.67–100.00)	0.029
GHS	75.00 (50.00–83.33)	58.33 (50–83.33)	0.291
Symptom scale			
Fatigue	11.11 (0–33.33)	33.33 (11.11–55.56)	0.022
Individual items			
Dyspnoea	0 (0–0)	33.33 (0–33.33)	0.033
Insomnia	0 (0–0)	0 (0–33.33)	0.009
EORTC QLQ-H&N35			
Pain	16.67 (0–75.00)	25.00 (0–66.67)	0.015
Swallowing	0 (0–41.67)	25.00 (0–66.67)	<0.001
Senses (taste and smell)	0 (0–100.00)	33.33 (0–100.00)	0.001
Speech	0 (0–77.78)	22.22 (0–66.67)	0.004
Eating in public	0 (0–50.00)	33.33 (0–100.00)	<0.001
Social contact	0 (0–73.33)	20.00 (0–73.33)	<0.001
Sexuality	0 (0–100.00)	66.67 (0–100.00)	0.045
Individual items			
Dental problems	33.33 (0–100.00)	66.67 (0–100.00)	0.028
Trismus	0 (0–100.00)	33.33 (0–100.00)	<0.001
Sticky saliva	33.33 (0–100.00)	66.67 (0–100.00)	0.021
Nutritional supplements	100.00 (0–100.00)	100.00 (0–100.00)	0.015

Mann-Whitney U test was used to assess differences. QoL, quality-of-life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GHS, global health status; EORTC QLQ-H&N35, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and neck cancer-35.

(Figure 1) are consistent with the literature (20).

Moreover, survival tends to be inversely related with tumoral stage (18). This relationship between cancer stage and QoL is also suggested by our data. In fact, despite most patients being diagnosed at advanced stages (III–IV), the majority of survivors presented with Stage I–II tumors at diagnosis.

Global health status of QoL and social functioning scores showed significant differences between local and metastatic groups in the QLQ-C30 questionnaire (Global health status of QoL 75 vs. 50 and social functioning: 100 vs. 66.6).

The H&N35 questionnaire was more sensitive in

finding differences between local and non-local groups. Swallowing, senses, speech, social eating, and social contact were significantly different for the analyzed groups. Infante-Cossio *et al.* (4) published similar results for 1-year follow-up oral cancer patients. Global health status of QoL was 70.8 and significant differences between local and locally advanced groups were described for pain, fatigue, appetite loss, speech, social contact, and social eating. Differences were also found for mouth opening, cough, weight loss, and pain management.

In fact, one of the biggest concerns of these patients is related to swallowing and eating in public. This item is

also highly stressed in the literature due to its high impact on their QoL (21,22). Moreover, its effect has been linked with the extent of resection and early diagnosis (23,24) and rehabilitation protocols designed to improve QoL after discharge. However, more studies are still required to assess the effects of rehabilitation in these type of patients (25).

On the other hand, pain, sexuality, and single-item analysis rendered non-significant results. These findings have also been published by other authors (23,24). What is more, Yang *et al.* described an improvement in pain, anxiety, and mood scores 1 year after treatment (24).

Moreover, several authors suggest a strong negative correlation between disease stage and QoL (5,26,27). Bjordal *et al.* (27) proposed a gradual decrease in QoL related to increasing stages of disease. These differences applied to virtually all symptoms and items in the QLC-C30 questionnaire. Apart from this, Stage I–II and stage III–IV groupings showed similar results, thus creating an important distinction between local and advanced tumors. To achieve a higher QoL discrimination, our patients were divided into three groups: local, locally advanced, and recurrent/metastatic.

Finally, our cohort included 11 patients with a recurrent or secondary lesion (18.33%). As a result, these patients required more aggressive treatments and developed worse functional outcomes. These findings are also consistent with other published papers (8).

A limitation of this study was that although several important variables were considered, such as stage of disease and whether or not adjuvant RT was given, other crucial variables were not. These included characteristics such as tumor site, type of flap used in reconstruction and cervical lymphadenectomy, all essential when evaluating QoL in these patients.

Radiotherapy

H&N35 is more affected by RT treatment than QLQ-C30. Significant differences were found in all groups and the following single items: Sticky saliva, dental problems, and trismus.

Tschudi *et al.* (12) published good QoL outcomes for oropharyngeal cancer patients that underwent curative treatment. H&N35 described higher differences than QLQ-C30, since RT effects are included in H&N35 in higher detail. Consequently, H&N35 has proven to be an effective tool in understanding the causes of secondary effects and changes in QoL after combined treatments.

Several transversal studies suggest that adjuvant RT may be correlated with lower functional scores and worse symptoms. Sticky saliva, dry mouth, and taste changes were highly correlated with RT treatment (26-29). Moreover, Infante-Cossio and Bjordal (4,27) stated that these symptoms could also be related with a higher stage of disease in these patients. Finally, RT side effects such as dermatitis, mucositis, muscular contraction, dental problems, and dry mouth clearly explain lower scores in QLQ-H&N35, since RT has been known to greatly impact QLQ-H&N35 symptom scores.

On the other hand, Baumann *et al.* (30) published that trismus may be a consequence of surgical interventions, while dry mouth caused by RT. Trismus could be related with higher resections required for oropharyngeal cancer, which may include pterygoid muscles (8).

Finally, when RT is combined with surgery, varying results have been published. Agarwal *et al.* (31) described an improvement in pain, stamina, leisure activities, mood, and anxiety levels. However, appearance, swallowing, chewing, speech, taste, shoulder pain and mouth dryness worsen.

López-Jornet *et al.* (32) published different results. Poorer results were found in patients treated only with surgery rather than surgery and RT. These results could be explained by the fact that tests were filled in the first year after treatment by some of the patients

Patient age

No significant association was found between QoL and patient age. Moreover, bibliography revision did not provide any conclusive results either.

On the one hand, some researchers have found higher QoL scores in elderly patients. Bjordal *et al.* (27) showed better emotional and social functioning in these patients. Torres-Carranza *et al.* (33) also found lower emotional and social functioning in younger patients. These findings might be related with longer life expectancy in younger adults. Hence, age should not be a contraindication for standard treatments. Operative and cognitive functions should be assessed instead. These could be achieved with performance scores such as the Karnofsky (15,34).

On the other hand, Dale *et al.* (29) found higher functioning scores in younger oropharynx cancer patients. López-Jornet *et al.* reproduced similar results and stated that these findings may be due to a higher comorbidity rate and aging effects in elderly patients (32). However, this cohort includes patients from all the Head and Neck area.

Finally, Bjordal *et al.* (27) found worse outcomes in physical performance, constipation, dyspnea, economic effects, teeth problems, dry mouth, cough, and sexuality.

Gender

Significant differences were found between genders in this study, with women scoring worse (higher) for pain, dry mouth, and sticky saliva in the EORTC QLQ-H&N35 survey, whereas female patients scored higher only for fatigue in the EORTC QLQ-C30 questionnaire. These results are somewhat consistent with other studies published (35). Nevertheless, there is some evidence that points to the contrary, generating some controversy on this matter (36).

Of all the items scored higher by women, dry mouth may be explained by menopausal dry mouth (37), at least when associated with RT. Boñar-Álvarez *et al.* found female sex to be an independent associated risk factor for hyposalivation before RT. Hence, being a male may act as a protective factor to prevent dry mouth (37).

Furthermore, higher survival rates have been found in female patients (17), which may be associated with and perhaps even explain these lower scores in QoL questionnaires. There are once again, however, discrepancies in results (38). In addition, many of the studies found during our literary review included broader terms such as “oral cancer” and “head and neck cancer”, thus limiting compatibility and comparison with our results.

Biases and guidelines for future research

Owing to its cross-sectional nature, survey filling ranges from 6 to 134 months after surgery (median =54 months). This could reduce symptom reports in patients that were assessed later and vice versa. Apart from this, results may also be altered by survival bias.

Infante-Cossio *et al.* (4) stated that 1 year follow-up is required to achieve stable symptoms. Hence, despite our reduced sampling consistency, the majority of our patients filled the questionnaires at least 1 year after treatment. Only 7 patients (all with local disease) were studied during the first year of follow-up. Moreover, similar results have been published by other authors (39,40).

Furthermore, we did not include a baseline pre-treatment questionnaire in our study, thus limiting our ability to calculate the impact of our treatments in the QoL.

Finally, these questionnaires may be quite time-consuming and may not accurately describe a patient's

suffering (41). Hence, adaptive tests have been developed regarding patients' characteristics. We believe these types of surveys would be the future in cancer QoL research.

Conclusions

QoL has become a crucial topic in cancer research. An initial problem when studying this topic was a lack of objective variables with which to evaluate and compare patients. Questionnaires such as H&N35 and QLQ-C30 serve as vital instruments in measuring and thus obtaining statistically comparable values. These metrics can also be used to give additional depth to other objective variables such as survival rates.

Patients treated with surgery for tongue cancer usually score highly in QoL questionnaires even in patients presenting locally advanced disease. However, cancer stage, adjuvant RT was shown to negatively affect QoL scores in almost every item measured. Out of the two questionnaires used in this study, the H&N35 questionnaire has been found to possess greater sensitivity in identifying these differences.

No differences for age were found, whereas higher scores for pain, dry mouth, sticky saliva and fatigue were found for women compared to men.

Finally, yet importantly, further steps in QoL understanding will arrive with larger, multi-center studies. This will allow for the development of greater cohorts with similar diseases, and to design personalized treatment protocols to improve survival and QoL outcomes.

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Footnote

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