

## Quality of life after treatment of laryngeal carcinoma: a single centre cross-sectional study

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### ABSTRACT

**INTRODUCTION** Laryngeal cancer treatment inherently affects life's most basic functions and significantly affects quality of life (QOL). We aimed to identify which aspects of QOL and which patients are most affected by the various treatment options.

**METHODS** The University of Washington Quality of Life (UW-QOL) questionnaire was administered to all patients with laryngeal cancer treated at a single institution over a seven-year period (2003–2010).

**RESULTS** In total, 41 patients responded. All had been treated for squamous cell carcinoma of the larynx. Questionnaires were completed at a median of 18.5 months after treatment. The overall quality of life was 81.1/100 as assessed by the UW-QOL scale, with only 4.9% reporting 'poor' or worse QOL. Neither patient age nor time after treatment significantly affected any aspect of QOL. Patients undergoing primary radiotherapy reported the best QOL. Those undergoing chemoradiotherapy or combined surgical treatment and chemoradiotherapy reported the worst QOL, particularly in terms of social eating, taste and saliva production. Patients with a T stage  $\geq 2$  and those with nodal metastases reported a significantly worse QOL.

**CONCLUSIONS** Overall, QOL in our patients was good. This study highlights the aspects of QOL most affected by various treatments for laryngeal cancer and identifies areas in which therapeutic intervention may be focused. It also provides information to guide clinicians when assisting patients to make informed decisions regarding treatment of their head and neck cancer.

### KEYWORDS

University Washington Quality of Life – Head and neck neoplasm

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The mainstays of treatment for head and neck cancers include surgery, chemotherapy and radiotherapy given alone or in combination. However, the side effects of these treatments are multifactorial in nature, causing substantial physical as well as psychosocial morbidity.<sup>1,2</sup> Their location inherently affects life's basic and vital functions including breathing, feeding and oral communication. Furthermore, altered appearance, difficulty in swallowing and pain as a result of treatment can cause problems with social function and have a further effect on a patient's quality of life (QOL).<sup>3</sup>

A number of studies have revealed QOL is affected by T and N stage,<sup>4,5</sup> time after treatment and treatment modality.<sup>5–7</sup> Investigation into the effect of these factors on specific aspects of QOL such as saliva production and swallowing has yielded varying conclusions.<sup>7–10</sup>

The aim of this study was to identify whether factors including patient age, treatment modality, tumour stage and nodal status significantly affect quality of life in patients treated for laryngeal cancer. It was hypothesised that patients with advanced T stage and nodal disease would experience poorer QOL. Furthermore, patients undergoing surgical treatment with or without chemoradiotherapy

would experience poorer QOL than those undergoing primary radiotherapy.

We aimed to identify those aspects of QOL that are significantly affected in order to counsel patients regarding the significant risks and benefits of treatment with uncertain curative outcomes. Furthermore, we aimed to identify patients at risk of significant side effects before treatment in order to effectively prepare them for their treatment experience and focus support from health professionals on the appropriate patients.

### Methods

The University of Washington Quality of Life (UW-QOL) questionnaire is a validated tool for determining QOL outcomes in patients treated for head and neck cancer.<sup>9,11,12</sup> We used version 3 of the questionnaire (the most current at the time), which consists of ten domain specific questions that ask patients regarding their experiences of pain, appearance, activity level, recreation, swallowing, chewing, speech, shoulder function, taste and saliva production in the last seven days, compared to the month before they developed cancer. Responses are marked from 0 (worst QOL)

**Table 1** Description and comparison of patients responding/not responding to the questionnaire

Demographic	Responders (n=41)	Non-responders (n=67)
Mean age	69.9 years	66.5 years
Tumour stage		
T1	41% (n=17)	30% (n=20)
T2	20% (n=8)	21% (n=14)
T3	24% (n=10)	28% (n=19)
T4	15% (n=6)	21% (n=14)
Treatment received		
Combined modality (surgery + chemotherapy and/or radiotherapy)	27% (n=11)	25% (n=17)
Primary radiotherapy	63% (n=26)	52% (n=35)
Chemoradiotherapy	10% (n=4)	22% (n=15)

to 100 (best QOL) based on validated scoring criteria. The mean score from the ten questions provides a composite global score.

An additional four questions specific to head and neck cancer asked patients to rate their QOL in terms of nausea, lymphoedema, social eating and sticky secretions. Two further questions asked patients to rate their current overall health and overall QOL compared to before they were diagnosed as well as whether they had difficulty with quitting smoking, reducing alcohol intake and whether they had experienced any financial or emotional problems as a result of their treatment. These additional non-validated questions were included to gain further insight into areas of QOL related to head and neck cancer that are not specifically covered by the UW-QOL questionnaire.

Printed copies of the questionnaires were posted along with stamped addressed envelopes to all patients identified from the cancer services database as having been treated for laryngeal cancer at the Royal Gwent Hospital otolaryngology department between April 2005 and June 2010. Data were collected initially in June 2006 for patients diagnosed between 2005 and 2006 and then subsequently for patients diagnosed between 2006 and 2010. A total of ten patients were excluded prior to sending questionnaires as they had either died or were in the terminal phases of illness.

Data were analysed using SPSS® version 15.0 (SPSS Inc, Chicago, IL, US) and statistical analyses were carried out using the Mann–Whitney U and Kruskal–Wallis tests after an initial analysis with the Kolmogorov–Smirnov test revealed the data to be non-parametric.

## Results

A total of 108 questionnaires were administered and 41 were returned completed. The reasons for non-participation

**Table 2** Mean quality of life score for all patients by domain

Domain	Score
Nausea	94.4
Pain	87.2
Appearance	85.9
Swallowing	87.1
Chewing	84.1
Lymphoedema	82.9
Shoulder function	82.6
Speech	81.4
Taste	78.9
Recreation	77.6
Activity	76.2
Social eating	74.3
Sticky secretions	70.8
Saliva production	69.9

were not disclosed by non-participants. All had been treated for squamous cell carcinoma of the larynx.

The mean age of the patients was 69.9 years (range: 52–90 years). There were 32 male and 9 female respondents. Questionnaires were completed at a median of 18.5 months after treatment (range: 2–55 months). Non-responders were comparable to responders in age, tumour stage and treatment received (Table 1).

The mean overall QOL for the entire group was 81.1/100 (range: 51–100). Self-reported QOL was high: 30 patients (73%) reported their QOL in the last 7 days compared to before treatment as ‘good’ or better, 9 (22%) reported ‘fair’ QOL and 2 (5%) reported ‘poor’ QOL. No patients reported their QOL as ‘very poor’.

The poorest domain in terms of QOL was saliva production whereas excellent QOL in terms of nausea was reported. The scores for each domain of the QOL questionnaire are shown in Table 2.

In terms of the additional questions, 12% of patients reported difficulty giving up smoking while no patients reported difficulty cutting down on alcohol intake. Furthermore, 12% of patients reported financial difficulty as a result of their treatment, 17% reported an increase in anxiety and 20% reported that they felt depressed as a result of their illness.

### Effect of age on quality of life

Patients were grouped according to whether they were above or below the median age (69.9 years). No significant differences in overall QOL or individual QOL domains were found between these groups. Moreover, patients over 75 years old were compared to those who were younger and again no significant differences emerged between these groups.

Table 3 Comparison of domains significantly affected by T stage

Domain	Median quality of life score (T≤2 : T>2)	Mean rank (Mann–Whitney U test)
Activity	85.5 : 67.3	23.8 : 16.9 ( $p<0.05$ )
Swallowing	92.1 : 80.2	23.7 : 16.7 ( $p<0.05$ )
Speech	89.0 : 74.6	23.7 : 16.7 ( $p<0.05$ )
Shoulder function	92.8 : 78.0	23.5 : 17.6 ( $p<0.05$ )
Taste	91.7 : 61.3	25.4 : 14.0 ( $p<0.01$ )
Saliva production	82.0 : 53.4	24.4 : 15.5 ( $p<0.01$ )

Table 4 Comparison of domains significantly affected by nodal disease positivity

Domain	Median quality of life score (N0 : N≥1)	Mean rank (Mann–Whitney U test)
Pain	92.1 : 62.5	22.9 : 11.2 ( $p<0.05$ )
Appearance	88.5 : 75.0	22.7 : 12.0 ( $p<0.05$ )
Swallowing	90.1 : 58.5	22.9 : 11.1 ( $p<0.05$ )
Chewing	89.1 : 37.5	23.1 : 9.9 ( $p<0.01$ )
Taste	86.0 : 41.5	23.3 : 8.1 ( $p<0.01$ )

### Effect of time

The median follow-up duration was 18.5 months. No aspects of QOL were significantly different between those who were followed up before or after this time. Furthermore, no significant differences in QOL emerged between those followed up before or after 12 months.

### Effect of TNM stage

Global QOL was significantly higher in patients with a T stage ≤2 (median global QOL: 90.1/100) compared to those with a T stage >2 (71.6/100) (mean rank: 26.2 : 12.8,  $p=0.001$ ). Advanced T stage was also associated with poorer QOL in several domains (Table 3).

Global QOL was significantly higher in patients without nodal disease (85.6/100) compared to those with nodal disease (55.4/100) (mean rank: 25.4 : 6.8,  $p=0.002$ ). Nodal disease was also associated with poorer QOL in several domains (Table 4).

### Effect of treatment modality

Global QOL was significantly higher in patients undergoing primary radiotherapy (median global QOL: 90.0/100) compared with combined treatment (71.6/100) and chemoradiotherapy (70.8/100) (mean rank [primary radiotherapy : combined treatment : chemoradiotherapy]: 26.4 : 14.1: 11.7,  $p<0.01$ ). Patients undergoing chemoradiotherapy or combined treatment reported significantly worse QOL in several domains compared to those undergoing primary radiotherapy (Table 5). Comparison between the chemoradiotherapy and combined modality groups revealed saliva production was significantly worse in patients undergoing chemoradiotherapy (median QOL: 16.5/100) compared

with those undergoing combined treatment (median QOL: 67.0/100) (mean rank: 3.5 : 9.4,  $p<0.01$ ).

Patients undergoing combined treatment appeared to report worse QOL in terms of speech, shoulder function and lymphoedema than those undergoing chemoradiotherapy but better QOL in terms of taste although these associations were not statistically significant.

### Discussion

Head and neck cancer patients are especially vulnerable as this type of cancer affects more than twice as many patients from the lower social class V than from the more affluent social classes I and II.<sup>15</sup> This may in part be explained by increased use of tobacco and alcohol in this group but other factors such as poor education are independently associated with increased risk of cancer.<sup>14</sup> This may reflect pre-existing difficulties with social integration.<sup>15</sup> Patients with head and neck cancer may therefore require increased support from health services when undergoing such demanding treatments to meet their QOL needs.

Overall, QOL in our group was high and comparable to similar published studies that reported mean QOL scores of between 70 and 85.<sup>4,6,8,9</sup>

We found no evidence of an effect of age on overall QOL. Khafif *et al* also found no differences in overall QOL between patients aged 75 or older when compared with younger counterparts.<sup>16</sup> However, they did suggest some subdomains of QOL were adversely affected by advanced age.

Previous longitudinal studies have demonstrated that QOL varies with time since surgery and have suggested there may be a dip in QOL between 0 and 6 months with an associated recovery after 12 months.<sup>4,5</sup> Our data failed to

Table 5 Comparison of domains significantly affected by treatment modality

Domain	Median quality of life score (primary radiotherapy : combined treatment : chemoradiotherapy)	Mean rank (Kruskal–Wallis test)
Speech	89.8 : 62.1 : 83.5	24.6 : 14.8 : 21.0 ( $p < 0.01$ )
Shoulder	93.1 : 67.0 : 91.7	24.6 : 13.8 : 24.0 ( $p < 0.05$ )
Taste	90.3 : 71.1 : 50.0	25.6 : 16.8 : 9.9 ( $p < 0.01$ )
Saliva production	81.3 : 67.0 : 16.5	24.9 : 19.8 : 4.25 ( $p < 0.01$ )
Lymphoedema	89.4 : 67.0 : 91.7	23.9 : 14.8 : 25.7 ( $p < 0.05$ )

support this conclusion; however, the cross-sectional nature of our study was not suited to this type of analysis.

Our data support the findings of El-Deiry *et al*, who found that T stage has a strong prognostic value for QOL one year after treatment of head and neck cancer.<sup>17</sup> Morton *et al* found that HNC patients with higher T stage tumours reported reduced overall QOL, with greatest significance being placed on difficulty swallowing and appetite.<sup>4</sup> Patients with higher N stage disease also reported reduced QOL, with the greatest significance placed on difficulty swallowing and head and neck pain.

Advanced T and N stage have also been associated with an increased risk of depression and, although this was not directly measured in our study, this factor should be considered when assessing and communicating with patients.<sup>18</sup> This is particularly important as QOL measurements are closely linked to patients' emotional status: in one study lower T and N stage were actually associated with poorer QOL as assessed by questionnaire.<sup>19</sup> It therefore follows that patients' perceptions of their illness may affect QOL as much as or even more than the physiological and anatomical extent of their disease.

As expected, patients undergoing primary radiotherapy reported better QOL in several domains when compared to those undergoing other treatment modalities. Lymphoedema, speech and shoulder function appeared to be better in the chemoradiotherapy group compared with the combined treatment group and, although this was not statistically significant, there is likely to be an effect of surgical neck dissection and subsequent mechanical disruption to the normal function of these areas, which could explain this association.

Although equal in terms of global QOL, patients undergoing chemoradiotherapy reported significantly worse QOL in terms of saliva production than those undergoing combined modality treatment.

Comparison of chemoradiotherapy and surgery for laryngeal tumours has yielded contrasting results in the literature. Tivedi *et al* found no difference in global QOL between surgery and chemoradiotherapy for treatment of advanced laryngeal cancers.<sup>20</sup> Xerostomia was significantly worse in the chemoradiotherapy group but surgically treated patients reported more difficulty with communication.

This corresponds to work by Boscolo-Rizzo *et al*, who found dry mouth and sticky saliva to be worse in those

receiving chemoradiotherapy.<sup>21</sup> However, this group found chemoradiation to be superior in terms of global QOL, speech and social contact compared to those undergoing surgical treatment.

Xerostomia as a result of radiotherapy is a significant burden on QOL<sup>22</sup> and represented the most common chemotherapy related toxicity after six months in a large study by Tobias *et al*.<sup>25</sup> Taste was worst affected in our chemoradiotherapy group but this did not reach statistical significance.

Targeted therapies (eg intensity modulated radiotherapy) have been proposed to reduce side effects such as xerostomia<sup>24</sup> and this was offered to patients locally subsequent to the completion of our study. Furthermore, advances in biological therapies including the use of monoclonal antibodies may potentially reduce the necessary dose of chemoradiotherapy.<sup>25</sup> Although this treatment is not offered locally, it is a consideration for the future and therefore further work will be required to investigate the effect of this on our population.

In most cases, the treatment administered to patients is dependent on the TNM stage of the tumour. Analysis of the T and N stage independently of treatment modality is therefore likely to reflect not just the effect of these factors but also the morbidity effect of the treatment given. Due to the relatively rare nature of these tumours, it is difficult to collect a large enough data set to allow a fully independent multivariate analysis of these factors and it was not feasible in this study due to the relatively small number of cases available for analysis. This is a recognised limitation of our study and has also been the experience of other investigators.<sup>26</sup>

This is important because these treatments have a significant impact on many aspects of QOL and the various treatment modalities need to be considered in the light of data regarding recurrence and survival, especially as patients are more likely to choose the option with the best chance of a cure regardless of the side effects experienced.<sup>27</sup> The response rate to this questionnaire was only 40% and this may also introduce bias into the results. The epidemiology of head and neck cancer has already been commented on and it is possible that this may affect response rates to questionnaires in this patient group. Furthermore, patients may be more likely to respond if they have experienced very good or very poor QOL following treatment and the results should therefore be interpreted in this light.

## Conclusions

The data presented provide a useful resource for healthcare professionals seeking to counsel patients regarding the expected side effects and highlight areas where intervention could be focused in the light of the stage of a patient's disease and the treatment offered.

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