Comparison of quality of life in advanced laryngeal cancer patients after concurrent chemoradiotherapy vs total laryngectomy

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OBJECTIVE: To compare quality of life (QOL) of patients with advanced laryngeal cancers treated by total laryngectomy with those who received concurrent chemoradiotherapy.

STUDY DESIGN: This is a cross-sectional study of the patients treated in our institution who have completed one year of follow-up and were disease-free at the time of evaluation.

SUBJECTS AND METHOD: Forty patients treated for advanced cancer of the larynx (stage III/IV), either by concurrent chemoradiation (11) or total laryngectomy and postoperative radiation (29), have been included in this study. The Functional Assessment of Cancer Therapy–Head and Neck (FACT–H&N) version 4 questionnaire was used.

RESULTS: Total scores for overall QOL are equal in both treatment groups \( (P = 0.69) \). Scores for individual components are similar in both treatment groups. However, dryness of mouth is significantly worse in the chemoradiotherapy group \( (P = 0.01) \) and ability to communicate with others is poorer in the laryngectomy group \( (P = 0.03) \).

CONCLUSION: Long-term overall QOL remains similar in all the patients treated for advanced carcinoma of the larynx irrespective of treatment modality.

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Current treatment protocols for advanced laryngeal carcinoma include either concurrent chemoradiotherapy (CTRT) or total laryngectomy and postoperative radiation (TL+XRT). The addition of chemotherapy to radiotherapy in organ preservation protocols has improved the larynx preservation rate.\(^1\) With comparable control rates for both treatment protocols, the relative impact of each treatment option on the patient’s quality of life (QOL) becomes critical in selecting the optimal modality. The sequela of treatment is different in both these groups. Patients receiving CTRT suffer from complications of chemotherapy and acute toxicities of radiotherapy, the intensity of which is greatly enhanced by the concurrent chemotherapy. The patients undergoing surgical treatment have to bear with the disability of having a permanent tracheostoma and loss of natural speech mechanism. They are also at risk of developing postoperative complications like pharyngeal leaks and shoulder dysfunction.\(^2\)\(^-\)\(^4\)

QOL is defined as satisfaction and well-being that a patient experiences on a daily basis.\(^5\) Most studies on QOL issues in head and neck cancer have included patients with cancer of different subsites in the head and neck region. However, the functional or cosmetic compromises vary with the site of the primary tumor in the head and neck, the stage of tumor, and the treatment modality, and hence these factors greatly influence the QOL. Very few studies have been reported on QOL outcomes after the treatment of cancer of the larynx. Cancer of the larynx and its treatment has significant impact on functions like speech and swallowing and hence on the QOL. Some early studies have reported on QOL in patients with cancer of the larynx after treatment using single-modality treatment in the form of surgery, radiotherapy, or chemotherapy, with no comparison being made on the outcome between the different treatment modalities.\(^6\)\(^-\)\(^8\) Other studies have compared the outcome after laryngectomy with radiotherapy alone,\(^7\)\(^,\)\(^9\) or neoadjuvant chemotherapy and radiation with laryngectomy.\(^10\) QOL outcomes after CTRT with TL+XRT, which is the current standard of care in advanced laryngeal cancers,\(^3\)\(^,\)\(^11\)\(^,\)\(^12\) have been directly compared in only three published studies.

The objective of this study is to compare the QOL outcome in patients with advanced laryngeal cancer after treatment with two different modalities of treatment, namely CTRT and TL+XRT, using the Functional Assess-
Materials and Methods

Patients
All patients with stage III or IV laryngeal cancer who were treated with a curative intent at the Amrita Institute of Medical Sciences, Kochi, a tertiary care cancer center, either by CTRT or by TL+XRT from February 2003 to December 2006, and who had completed one year of disease-free follow-up, were included in this study. Institutional review board approval was obtained for conducting a prospective evaluation of the QOL of these patients using the FACT–H&N tools.

Patients with thyroid cartilage erosion were offered TL+XRT, while patients with poor performance status (Karnofsky’s performance status scores [KPS scores] < 80) were not considered for CTRT. For all other patients, both treatment options were discussed with the family and final decision was taken. Surgical treatment included total laryngectomy with or without partial pharyngectomy and tracheo-esophageal prosthesis (TEP) insertion. This was followed by standard fractionation radiotherapy (2 Gy/day, 5 days/week, total 60–66 Gy). Patients who received CTRT received standard fractionation radiotherapy (2 Gy/day, 5 days/week, total 66–72 Gy) with concurrent chemotherapy using cisplatin. Chemotherapy was given as cisplatin 100 mg/m² at weeks 1, 4, and 7. All patients received at least two cycles of chemotherapy.

QOL Measures
All patients eligible for study were asked to complete FACT–H&N version 4 quality-of-life questionnaires. The Malayalam (local language) version of FACT–H&N version 4 has been validated. Patients could choose either the Malayalam or English version. The medical-social worker administered the questionnaire.

The FACT–H&N version 4 QOL instrument consists of five components: physical well-being, social/family well-being, emotional well-being, functional well-being, and additional concerns. Each component has statements with a choice of five responses, from 0, which means “not at all” to 4, which means “very much.” The patient has to mark his or her choice of response. For a positive statement, like “I feel close to my friends,” the response 4 represents a good response and is calculated as 4 in the scoring. However, for a negative statement like “I have pain,” a response of 4 (very much) actually means poor response and hence the score needs to be reversed. In this case, the score is derived by subtracting the item response from 4 (4 – item response, ie, 4 – 4 = 0). The scores for all statements in each component of the questionnaire are added together to get the overall score of that component. Higher score represents better outcome.

The component “additional concerns” tests issues specific to head and neck cancer and its treatment, like ability to eat food, dryness of mouth, breathing, quality of voice, swallowing, disfigurement, ability to communicate in public, and pain in face-throat-shoulder. This provides an opportunity to evaluate site- and treatment-specific issues.

Statistical Analysis
The scores of the QOL were calculated according to the FACT–H&N scoring manual. Statistical analysis was performed using the SPSS/PC software package (SPCC, Inc, Chicago, IL). Student t test and Fisher exact test were used to test the statistical significances of difference in mean values of physical, social, emotional, and functional well-being and total QOL scores. The χ² test was applied to test the statistical significance of the differences in the proportion of cases with score ≥2, between the two treatment groups. Tests were two-tailed and the level of statistical significance was calculated at the 5 percent level of probability.

Results
Forty patients with stage III or IV laryngeal cancer treated with curative intent completed the QOL evaluation instrument. Eleven patients received CTRT and 29 patients underwent TL+XRT. Demographic characteristics of both treatment groups are listed in Table 1. Analysis suggested no significant differences among the two groups regarding age (P = 0.88), gender (P = 0.12), stage (P = 0.48), or performance status (P = 0.75). All patients had completed at least one year of disease-free follow-up after their treatment at the time of inclusion in the study. The mean duration after treatment at which the patient completed the questionnaire was 20 months (range, 12 to 34 months) in the CTRT group and 18 months (range, 6 to 30 months) in the TL+XRT group.

Table 1: Demographic characteristics of treatment groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TL+XRT</th>
<th>CTRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, range)</td>
<td>60.40 (48-73)</td>
<td>59.45 (36-78)</td>
</tr>
<tr>
<td>Sex, no.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>IV</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Karnofsky’s performance status scores (mean, range)</td>
<td>90 (70-100)</td>
<td>90 (80-100)</td>
</tr>
</tbody>
</table>

CTRT, concurrent chemoradiation; TL+XRT, total laryngectomy with postoperative radiotherapy.
group and 22 months (range, 12 to 31 months) in the TL/H11001 XRT group.

The mean scores of each component of the QOL questionnaire in the two groups of patients are shown in Table 2. The scores were almost equal in both treatment groups (Table 2), indicating good overall QOL in both groups. But in the head and neck–specific additional concerns group, lower scores were obtained in a few areas. Table 3 shows the scores of individual issues in the head and neck–specific additional concerns group. Scores greater than 2 were considered as good response and scores equal to or less than 2 were considered as bad response. Dryness of mouth was an issue of concern for patients receiving CTRT, and this difference was statistically significant compared to the TL/H11001 XRT group ($P = 0.01$). Ability to communicate with others was significantly better in the CTRT group than in the TL/H11001 XRT group ($P = 0.03$). Most of the patients in both groups felt that they had lost their usual quality and strength of voice. A number of patients in this series had developed pharyngeal stricture and had problems with their swallowing. Most patients in both groups were happy with their appearance (Table 3).

### DISCUSSION

QOL is broadly defined as an individual’s perception of overall well-being. It mainly has two aspects, individuality and multidimensionality. Individuality implies that the patient’s perception of good health is more important than the physician’s perception. The second aspect is related to the multidimensional nature of health. Overall well-being is related not only to the disease status and treatment but also to its social, emotional, functional, and economic impacts on the individual. Any instrument that measures QOL of patient should include all these different components to have a comprehensive assessment.

### Table 2

Results from Functional Assessment of Cancer Therapy–Head and Neck (FACT–H&N) version 4 quality-of-life questionnaire: Scores for different components and total score

<table>
<thead>
<tr>
<th>Scale</th>
<th>Chemoradiation</th>
<th>TL+XRT</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical well-being</td>
<td>20.45</td>
<td>20.28</td>
<td>0.91</td>
</tr>
<tr>
<td>Social well-being</td>
<td>22.38</td>
<td>21.75</td>
<td>0.67</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>19.55</td>
<td>19.02</td>
<td>0.77</td>
</tr>
<tr>
<td>Functional well-being</td>
<td>19.82</td>
<td>18.93</td>
<td>0.75</td>
</tr>
<tr>
<td>Head and neck–specific additional concerns</td>
<td>19.27</td>
<td>18.67</td>
<td>0.74</td>
</tr>
<tr>
<td>Total scores</td>
<td>101.47</td>
<td>98.66</td>
<td>0.69</td>
</tr>
</tbody>
</table>

*SD, standard deviation; TL+XRT, total laryngectomy with postoperative radiotherapy.*

### Table 3

Results from Functional Assessment of Cancer Therapy–Head and Neck (FACT–H&N) version 4 quality-of-life questionnaire: Distribution of patients according to response for each question

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Chemoradiation</th>
<th>TL+XRT</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Good*</td>
<td>Bad†</td>
<td>Good*</td>
</tr>
<tr>
<td></td>
<td>No. of patients</td>
<td>No. of patients</td>
<td>No. of patients</td>
</tr>
<tr>
<td>Ability to eat all types of food</td>
<td>5</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Dryness of mouth</td>
<td>2</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Breathing</td>
<td>10</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Voice quality and strength</td>
<td>2</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Quantity of food</td>
<td>5</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Appearance</td>
<td>6</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Swallowing</td>
<td>4</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Communication</td>
<td>9</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Pain</td>
<td>4</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

*TL+XRT, total laryngectomy with postoperative radiotherapy.*

*Good = scores $>2$.

†Bad = scores $\leq 2$. 
In the last few years, many comprehensive QOL instruments have been validated and become available for use in clinical practice. Health-related QOL instruments could be divided into general or disease-specific instruments. General instruments contain multiple general domains like physical well-being, social well-being, emotional well-being, and economic well-being. They assess the impact of patients’ health on their overall QOL combining all these parameters. Their main advantage is that they can be used for different clinical conditions and the results can be compared over a broad spectrum. Their main limitation is the inability to focus on specific issues regarding different disease process, treatment, or different subsites. Examples of general QOL instruments are the Medical Outcome Study (MOS) and 36-Item Short-Form Health Survey (SF-36). 

Disease-specific instruments focus on specific issues concerning that particular disease and allow better comparison between similar patient groups. For cancer patients, different QOL instruments are available, such as the Functional Assessment of Cancer Therapy (FACT) scale and the Functional Living Index-Cancer (FLIC). They provide better outcome assessment than general instruments regarding that particular disease.

Patients with head and neck cancer have significant functional and cosmetic problems specific to the primary site of cancer. Instruments that can specifically address these issues will be helpful in knowing the effect of different treatment modalities on these specific functions. This eventually helps us to select optimal treatment modalities among different available options. A few specific instruments are devised for head and neck cancer, like the University of Washington Head and Neck Cancer Questionnaire (UW-QOL), Performance Status Scale for Head and Neck Cancer Patients (PSS-HN), and the University of Michigan Head and Neck QOL questionnaire. The impact of treatment-related toxicities on QOL could be assessed using treatment-specific QOL questionnaires such as the Head and Neck Radiation Therapy Questionnaire (HNRQ). Evaluation with these instruments enables us to introduce minor modifications in our treatment, which can have major impact on a particular symptom and ultimately improve the final outcome.

FACT–H&N version 4 has general domains in the form of physical, social, emotional, and functional well-being and, in addition to this, a separate domain of additional concerns, which specifically deals with issues related to head and neck cancer. This “combined” approach provides an opportunity for comprehensive assessment of patients’ overall as well as disease-specific QOL. FACT is a multidimensional QOL questionnaire that has been validated and found reliable. It is validated in many languages including Malayalam, which is a local language in this geographic location. FACT–H&N version 4 has been validated for head and neck cancer patients. Though other QOL questionnaires have been used to evaluate QOL-related treatment outcome in patients with carcinoma of the larynx, FACT–H&N version 4 is still not used, and this study gives us an opportunity to compare this instrument with other instruments and assess its feasibility for future use.

Two other frequently used QOL instruments are the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ) and the University of Washington QOL (UW-QOL) instrument. EORTC QLQ used for head and neck consists of two components, the core questionnaire (QLQ-C30) and the head and neck module (QLQ-H&N35). A core instrument contains six subscales with 30 items, while the head and neck questionnaire contains 35 items, seven multiple-item scales, and 10 single-item scales pertaining to head and neck-related issues. The UW-QOL instrument is composed of three parts. The first section consists of 12 domains that pertain to the degree of QOL in the categories of pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety. The second part of the instrument asks patients which issues have been the most important to them in the past seven days. In the final part of the instrument, patients are given three general questions comparing the following: 1) current health-related QOL to one month before developing cancer; 2) health-related QOL during the past seven days; and 3) overall QOL during the past seven days.

Many social, emotional, economic, and physical issues depend on culture, society, and upbringing of individual and religious beliefs. These things show great variance from region to region, and the impact of disease and its treatment on a patient’s overall QOL may be different accordingly. Literature regarding QOL in Indian cancer population is very sparse. A questionnaire for Indian cancer patients was validated by Vidhubala et al, in which they highlighted factors contributing to QOL in Indian scenarios. The 10 factors that emerged were psychological well-being, self-adequacy, physical well-being, confidence in self-ability, external support, pain, mobility, optimism and belief, interpersonal relationships, and self-sufficiency and independence. There is no study carried out for Indian populations for carcinoma of the larynx before this. Our aim is to evaluate the impact of treatment for carcinoma of the larynx on QOL in this group of patients.

In the present study, scores for overall QOL were equal and in the higher range in both treatment groups. This indicates that patients had good long-term overall QOL irrespective of treatment modality. This finding confirms the trend observed in other reported studies. Separate analyses of the scores of the different components of the questionnaire also show no significant difference between the two treatment groups. This finding is in contrast to some of the studies that have been published. In a recently published series, Boscolo-Rizzo et al showed that physical, social, and functional scores were better in the CTRT group. Hanna et al and the Veterans Affairs Laryngeal Cancer Study Group also suggested that patients in the TL+XRT
group showed a trend towards more disruptive social functioning than in the CTRT group. They believed that increased pain, disfigurement, disrupted body image, social anxiety, or impairment of speech might be the main contributing factors for these low scores in the surgery group.

In our study, we had equal scores for physical, social (family), and emotional well-being for both arms. Liberal use of TEP in the TL+XRT group, well-planned speech rehabilitation, and good counseling involving those close to the patients may have contributed to improved speech outcomes in the surgery group in our study. In India, there is a very strong and closely knit social support system in the form of family members and relatives. Hence, the anxiety of social acceptance after total laryngectomy may not be a very big problem here, which was reflected in comparable social and functional scores between both groups. Moreover, after undergoing lengthy cancer treatment and long follow-up, the patient’s outlook and expectation for himself and life changes, and the patient may become adapted to his appearance; hence, disfigurement may not contribute to patients’ overall QOL in the longer term.

There are few significant differences in the outcome when head and neck cancer treatment-specific questions are compared between the two groups. The most notable side effect of chemoradiation is dryness of mouth and sticky saliva, which may be due to the radiosensitization effect of the chemotherapy. There was a statistically significant difference when this issue was addressed between the two groups, with the CTRT group faring poorly.

The main advantage of larynx preservation with CTRT is a better speech outcome. Use of TEP in total laryngectomy patients allowed good phonation in most of the patients, but the ability to fluently communicate with others was found to be better in patients with intact larynx in the CTRT group. Other head and neck-specific issues asked in the questionnaire pertaining to taste, swallowing, ability to eat solid food, pain, cosmesis, and breathing were found to be equal in both groups.

This study has certain limitations. The small number of the patient population and uneven patient distribution between both groups make it difficult to obtain statistically significant conclusions. The study is nonrandomized in nature and a point prevalence survey. Though our analysis suggested no significant differences among two groups regarding age, gender, stage, or performance status, due to its nonrandomized nature, many factors might have influenced selection of patients in different treatment groups that could have influenced the ultimate QOL outcome. There is no comparison between pretreatment QOL scores and post-treatment QOL scores as well as assessment of QOL at different time intervals, which would have given a complete view of the patient’s status at different times of treatment.

This is the first study using the FACT-H&N version 4 QOL instrument in an Indian population for assessment of QOL in patients with laryngeal cancers undergoing different modalities of treatment. Though statistically significant conclusions are difficult to make, this study shows some trend in patient outcome and forms a basis for future prospective studies. The results of the study show that contrary to the perceptions, the overall QOL outcome remains the same, and good, irrespective of the treatment modality adopted. But specific issues related to functional disabilities vary with the modalities, and this fact has to be taken into consideration and discussed with the patient before making treatment decisions. Further prospective and randomized studies would be needed to provide more definite answers that can aid decision-making.

CONCLUSION

Patients with stage III and IV laryngeal cancer have good long-term overall QOL outcomes, regardless of the modality of treatment received. Patients in the CTRT group had worse outcome regarding dryness of mouth and TL+XRT patients had worse outcome in the domain of ability to communicate with others. Outcomes regarding physical well-being, social well-being, emotional well-being, and functional well-being remained equal in both of the treatment groups.

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AUTHOR CONTRIBUTIONS

Dr Subramania Iyer, study design, final manuscript; Dr Nirav P. Trivedi, study design, data collection, analysis, writing of manuscript; Dhanya Kalathungal Swaminathan, data collection; Dr Krishnakumar Thankappan, literature review, analysis; Dr Shilpa S. Chatni, literature review, analysis; Dr Moni A. Kuriakose, study design, final manuscript.

FINANCIAL DISCLOSURE

None.
REFERENCES