Life After Total Laryngectomy

A Measure of Long-term Survival, Function, and Quality of Life

Troy D. Woodard, MD; Agnes Oplatek, MD; Guy J. Petruzzelli, MD, PhD, MBA

Objectives: To analyze postoperative clinical, functional, and quality-of-life (QOL) outcomes in patients after total laryngectomy (TL) and to determine the effect of preoperative variables (including age, sex, comorbidities, prior chemotherapy or radiation therapy, and tumor site and stage) on long-term survival and quality of life.

Design: We performed a retrospective cohort follow-up study of patients who underwent TL for cancer between July 28, 1994, and August 11, 2005.

Setting: University tertiary care facility.

Patients: One hundred forty-three patients who underwent TL were identified, and their hospital medical records were reviewed. Ninety-one patients (63.6%) underwent TL for primary carcinoma and 52 (36.4%) for recurrent cancer. At follow-up, 58 patients (40.6%) were alive.

Main Outcome Measures: Baseline characteristics and preoperative clinical variables were collected. Follow-up data on function and QOL were collected from patients who were alive at the time of study via the Head and Neck Cancer Inventory, a previously validated questionnaire. Survival was estimated using the Kaplan-Meier method. Univariate and multivariate analysis was used to determine factors significant for survival.

Results: The overall median survival for the cohort was 23.0 months (mean ± SD, 50 ± 29 months). On univariate analysis, the following 5 factors were significant predictors of long-term survival: cancer site in the larynx, T3 stage, N0 to N1 stage, presence of no more than 2 comorbidities, and absence of cardiovascular comorbidities at the time of cancer diagnosis (P < .05). On multivariate analysis, only T stage maintained significance as a predictor of survival (P = .04), while cancer site was nonsignificant at P = .07. For patients alive at the time of study, functional and QOL outcomes for 5 domains (speech, eating, social disruption, aesthetics, and overall QOL) ranged from intermediate (score, 31-69) to high (score, 70-100) categories. Pretreatment patient-related factors that correlated with notably better functional and QOL outcomes in at least 1 domain were age older than 65 years at diagnosis, presence of no more than 2 comorbidities, no history of previous chemoradiation therapy, and primary tracheoesophageal puncture placement.

Conclusions: Pretreatment clinical variables (including primary tumor site, tumor stage, regional metastases, and number and type of comorbidities) have an effect on long-term survival after TL. Despite common belief, many patients who have undergone TL maintain a good QOL overall. This study sheds light on which patient-related factors may affect health-related QOL outcomes after TL. These findings may be used to select patients who are good candidates for TL based on anticipated functional and QOL outcomes.

Arch Otolaryngol Head Neck Surg. 2007;133:526-532

Cancer of the head and neck accounts for 4% of new malignant neoplasms diagnosed in the United States each year. While the most common risk factors include tobacco and alcohol use, anyone can become affected. The American Cancer Society estimated that approximately 66,000 new cases of upper aerodigestive cancer were diagnosed in 2004. Of those, 10,270 cases involved the larynx, and 2,500 cases were in the hypopharynx. This makes laryngeal cancer the second most common upper aerodigestive cancer.

The male-female incidence of laryngeal cancer has fallen from 15:1 to less than 5:1. An increase in women’s use of tobacco products and their heightened exposure to carcinogens in the environment has led to the dramatic change in its prevalence. Laryngeal cancer is twice as likely to be present in black subjects than in white subjects and is more likely to be diagnosed at a later stage.

CME course available at www.archoto.com

Head and neck cancer, particularly laryngeal cancer causes pain and dysphagia and impedes speech, breathing, and social interactions. The perception is that total laryngectomy (TL) is disabling and
has a detrimental effect on an individual’s quality of life (QOL).

Despite many advances in treatment, there has not been a dramatic change in the overall survival of patients with advanced-stage cancer. Over time, the treatment regimens for laryngeal and hypopharyngeal cancer have shifted from traditional radical surgery to less destructive larynx-preserving surgery. During the last 2 decades, chemotherapy and radiation therapy (RT) have been incorporated into treatment protocols. These forms of therapy have demonstrated no statistically significant differences in survival rates. Two large randomized clinical trials showed that treating patients with advanced-stage laryngeal cancer using induction chemotherapy followed by RT can achieve laryngeal preservation without negatively affecting survival.2,3

For many patients who would otherwise undergo TL for their advanced-stage cancer, this treatment seems to be a viable option for preserving their larynx. However, induction chemotherapy with RT is not an option for every patient. The toxic effects, which include but are not limited to severe nausea, fatigue, mucositis, renal damage, otologic damage, and suppression of the hematopoietic and immune system, place many patients at risk of significant morbidity.4

In addition, the mere presence of a preserved larynx does not ensure its function. The exposure to chemotherapeutic agents and RT results in pain, dysphagia, and continued speech disturbances that are associated with posttreatment edema and fibrosis.4,5

Although some tumors respond to primary chemoradiation therapy, there are many cases in which the tumor does not respond and is only susceptible to salvage surgical resection. In addition, patients with poor pulmonary reserve and laryngeal function after curative chemoradiation therapy are at high risk for developing aspiration pneumonia.5,6 Therefore, TL for prevention of aspiration would be beneficial.

The gradual trend toward larynx-preserving therapy in advanced-stage laryngeal and hypopharyngeal cancer has led to much controversy about which option is best for patients. Although some studies2,3 show no survival difference between standard surgery with postoperative RT and induction chemotherapy with RT, other studies5,7-10 differ in regard to functional outcomes and health-related QOL. There is a scarcity of long-term functional status and QOL data about patients who have undergone TL. It is important for health care providers to have a better understanding of what pretreatment factors may affect survival, postoperative functional outcome, and overall QOL.

**RESULTS**

Patient characteristics are given in Table 1. One hundred forty-three patients were identified. The age at diagnosis ranged from 35 to 90 years, with a mean age of 63 years. There were 120 men and 23 women. The primary site of tumor was isolated to the larynx in 92 patients, was confined to the hypopharynx in 44 patients, and was synchronous in 7 patients. At the time of follow-up, 58 patients were alive. The mean follow-up for the living patients was 37 months (range, 7-110 months).

Five patients (5.6%) had T2 disease, 44 patients (49.4%) had T3 disease, and 40 patients (44.9%) had T4 disease, and T stage was unknown for 2 patients of 89 patients with primary tumors. Fourteen patients (30.4%) of 46 patients with recurrent cancer had T1-2 disease, 32 patients (69.6%) had T3-4 disease, and the T stage was unknown for 6 patients (Table 1). Fifty-two patients (36.4% of all patients) had previous RT. Of 120 patients with known nodal disease, the deceased patients were more likely to have had N2 to N3 disease than the living patients (72.7% vs 27.3%, P = .005). There was also a statistically significant difference in the length of hospital stay. The deceased patients were in the hospital on average 3.5 more days than the living patients (mean ± SD, 9.5 ± 9.1 vs 6.0 ± 3.5 days, P = .006).

Table 2 gives the pathological staging of the patients who received primary surgical therapy and of those who experienced recurrent disease.

The overall median survival among 143 patients was 23.0 months (mean ± SD, 50 ± 29 months). While patients with primary cancers located in the larynx had a
median survival of 42 months, those with cancers located in the hypopharynx and those with synchronous cancers had significantly shorter 5-year median survival (16 and 10 months, respectively; \( P = .005 \)) (Figure 1).

Patients with more advanced-stage tumors (T4) and those with recurrent tumors had lower 5-year survival compared with that of patients with T3 tumors (median survival, 21 and 23 months, respectively, vs 58 months; \( P = .03 \)) (Figure 2). Patients with N2 or greater regional neck metastasis also had significantly shorter median survival than patients with N1 or less neck disease (23 months vs 50 months, respectively, \( P = .005 \)).

On univariate analysis, patients with more than 2 comorbidities had lower survival rates (\( P = .02 \)) (Table 3). In addition, the presence of cardiovascular comorbidities was associated with significantly decreased 5-year survival (\( P = .04 \)).

The overall incidence of postoperative complications in our study was 18%. Complications were more likely to occur in patients who had RT before surgery (\( P = .003 \)) (Figure 3). Among patients with postoperative complications, pharyngocutaneous fistulae occurred in 32%
of patients with previous RT vs in 12% of patients without previous RT.

Thirty-three (56.9%) of 58 patients completed the self-administered Head and Neck Cancer Inventory. The mean overall QOL scores in each domain (speech, eating, social disruption, and aesthetics) were 56, 69, 78, and 72, respectively (Table 4). The scores signify that these patients had QOL outcomes within the intermediate (score, 31-69) and high (score, 70-100) categories.

Table 5 gives the functional and QOL outcomes. Patients older than 65 years (n=18) had statistically higher outcomes in all 4 domains. In addition, their mean overall QOL score was significantly higher than that of patients 65 years or younger (score, 75 vs 54). There was no difference in QOL outcomes based on T stage. However, patients with no more than 2 comorbidities had significantly higher scores on social disruption attitude. These patients had higher functional and attitudinal scores in each domain. Patients who did not undergo chemoradiation therapy before surgery had significantly better eating outcomes. They had higher scores in the social disruption, aesthetics, and overall categories compared with patients who had prior chemoradiation therapy. When comparing primary (n=26) vs secondary (n=7) tracheoesophageal puncture (TEP) placement in patients, there were significant differences in functional outcomes. Primary TEP placement resulted in better eating and overall functional outcomes. In addition, there was better mean overall QOL among patients with primary TEP placement.

**COMMENT**

Although improving survival remains the primary goal in treating patients with head and neck cancer, laryngeal preservation has emerged as a viable alternative to radical surgery. Despite this attempt to maintain a functional larynx, many patients will inevitably require TL...
Eating Overall Aesthetics Social Disruption
tasize to regional lymph nodes. pharyngeal tumors have a greater propensity to metas-
stage. In addition, compared with glottic tumors, hypo-
from their general late presentation at a more advanced
survival in patients with hypopharyngeal tumors stems
of our patients was similar. It is thought that decreased
and hypopharyngeal cancer range from 42% to 67% and
outcomes.
mine whether any pretreatment factors affect these
objective of this study was not only to assess clinical
and use available data to provide a more compre-
ion) remedy. It is important that health care providers
obtain a better understanding of patients’ health-related
QOL and use available data to provide a more compre-
sive approach to patients’ medical care. Therefore, the

The 5-year survival rates of advanced-stage laryngeal
and hypopharyngeal cancer range from 42% to 67% and
from 19% to 42%, respectively. The survival rate
of our patients was similar. It is thought that decreased survival in patients with hypopharyngeal tumors stems from their general late presentation at a more advanced stage. In addition, compared with glottic tumors, hypopharyngeal tumors have a greater propensity to metastasize to regional lymph nodes.

Consistent with studies by Shah et al and Chen et
al, who demonstrated decreased survival in their patients with nodal metastasis, our data showed a substantial decrease in survival. Patients with N2 or greater neck disease lived, on average, 22 months less than those with N1 or less neck disease.

As expected, patients with T4 or recurrent tumors fared worse than patients with T3 disease. The median 5-year survival was 58 months (range, 34-82 months) for T3 lesions, 21 months (range, 8-34 months) for T4 lesions, and 23 months (range, 12-35 months) for recurrent lesions. This overall decreased survival among patients with recurrent disease suggests that recurrent tumors have the potential to be more aggressive. Although persistent or recurrent disease may result from inadequate primary therapy, it is also conceivable that these tumors were resistant to chemotherapy and RT. As a result, the previous treatment may have selected for a more aggressive or resistant strain of tumor cells.

Many of our patients had multiple comorbidities before surgery. The association of more than 2 comorbidities with a negative effect on survival raises a suspicion. Are we putting these patients at greater risk by operating on them? Based on our findings, the number or type of comorbidity had no effect on acute postoperative complications. However, they were significant predictors of long-term survival. The presence of more than 2 comorbidities can be used as a measure by the surgeon to aid in the preoperative selection of patients and to help determine which patients should undergo further medical clearance before surgery. Of the various comorbidities, only cardiovascular morbidities (eg, hypertension, coronary artery disease, diabetes mellitus, hyperlipidemia, and prior myocardial infarction) had a negative effect on 5-year survival. These findings are consistent with those of several studies. Chen et al and Piccirillo and colleagues identified 7 comorbidities (3 of which involved the cardiovascular system) that significantly decreased survival among their patients with head and neck cancer. Singh et al used the Charlson comorbidity index and found that patients with advanced comorbidities had a decrease in tumor-specific survival (12.3 months vs 38.7 months in patients with low-level comorbidities).

Postoperative complications were significantly greater in patients who had previous RT. In our series, postoperative complications, including wound infections and pharyngocutaneous fistulae, occurred in 51% of patients who had previous RT. Of those patients, approximately 31% had solely pharyngocutaneous fistulae formation, which is a well-documented complication. Grau et al examined 472 patients who underwent salvage laryngectomy after prior RT. In their 10-year review, they noted an increase in pha-

### Table 5. Patient-Related Factors and Quality of Life (QOL) Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>Speech</th>
<th>Eating</th>
<th>Social Disruption</th>
<th>Aesthetics</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65</td>
<td>15</td>
<td>46 ± 26*</td>
<td>45 ± 26*</td>
<td>55 ± 23*</td>
<td>62 ± 21</td>
</tr>
<tr>
<td>&gt;65</td>
<td>18</td>
<td>64 ± 18*</td>
<td>66 ± 22*</td>
<td>74 ± 17*</td>
<td>80 ± 21</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3-4</td>
<td>22</td>
<td>60 ± 24</td>
<td>61 ± 28</td>
<td>66 ± 24</td>
<td>74 ± 23</td>
</tr>
<tr>
<td>Recurrent</td>
<td>11</td>
<td>48 ± 21</td>
<td>48 ± 21</td>
<td>66 ± 18</td>
<td>68 ± 22</td>
</tr>
<tr>
<td>No. of comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>21</td>
<td>58 ± 23</td>
<td>58 ± 23</td>
<td>67 ± 18</td>
<td>73 ± 20</td>
</tr>
<tr>
<td>&gt;2</td>
<td>12</td>
<td>53 ± 25</td>
<td>54 ± 32</td>
<td>63 ± 28</td>
<td>70 ± 26</td>
</tr>
<tr>
<td>Previous radiation therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>23</td>
<td>58 ± 25</td>
<td>59 ± 28</td>
<td>66 ± 24</td>
<td>74 ± 22</td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
<td>51 ± 20</td>
<td>50 ± 20</td>
<td>65 ± 19</td>
<td>68 ± 23</td>
</tr>
<tr>
<td>Previous chemoradiation therapy</td>
<td>31</td>
<td>55 ± 23</td>
<td>56 ± 26</td>
<td>68 ± 21*</td>
<td>74 ± 21*</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>65 ± 42</td>
<td>60 ± 35</td>
<td>36 ± 15*</td>
<td>34 ± 12*</td>
</tr>
<tr>
<td>Yes</td>
<td>26</td>
<td>56 ± 24</td>
<td>57 ± 26</td>
<td>70 ± 20*</td>
<td>71 ± 24</td>
</tr>
<tr>
<td>Tracheal esophageal puncture</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>7</td>
<td>54 ± 26</td>
<td>55 ± 29</td>
<td>50 ± 26*</td>
<td>74 ± 16</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant at P<.05.
ryngocutaneous fistulae formation from 12% to 30%; the overall incidence was 21%. Other authors relate pharyngocutaneous fistulae formation to RT, with the observed incidence ranging from 9% to 35%.20

Radiation therapy causes tissue damage and leads to poor wound healing. However, the high number of associated postoperative complications may be a result of the broader gradual shift to intensify RT in patients with cancer. To validate this assumption, we must obtain the RT schedules and doses to see if there is a correlation with wound breakdown and pharyngocutaneous fistulae formation.

The high rate of pharyngocutaneous fistulae may also be due to poor nutrition in patients with cancer. Many of these patients have limited oral intake because of their extensive tumor burden. Measurement of serum albumin levels and initiation of tube feedings could be started early to prevent malnutrition.

There is a common presumption than laryngeal preservation with chemoradiation therapy results in better QOL compared with that of patients undergoing TL. Although the larynx may be preserved, numerous posttreatment complications may still result. Because QOL is a multidimensional phenomenon, it is important to use a validated instrument that considers various domains when measuring functional outcomes and QOL. There is a scarcity of long-term functional status and QOL data about patients who have undergone TL.

This study evaluated functional outcomes in the speech, eating, social disruption, and aesthetics domains in patients who underwent TL. In addition, an overall measure of QOL in these patients was obtained. Nevertheless, there are a few limitations to this study, such as the lack of a control group. The second limitation is that this study was performed retrospectively, and our QOL survey only included survivors. Third, there is potentially a component of survivorship effect.

Although our series did not have a control group, our results parallel those of previous findings by Funk et al7,11 and El-Deiry et al.8 They used the Head and Neck Cancer Inventory to compare QOL in patients receiving chemoradiation therapy with that in patients undergoing surgical resection followed by RT. They found no statistically significant QOL difference between the 2 groups. Similarly, our cohort of patients receiving surgical therapy had mean scores in each domain ranging from intermediate to high QOL. Predictably, the speech scores were the lowest of all domains. Considering that all of our patients had undergone TL, the finding of mean speech scores in the intermediate category is notable. Contrary to common thought, this demonstrates that these patients can have not only good functional speech but also a positive attitude about their speech. This finding is also in agreement with results by Stewart et al11 and Deleyiannis et al,9 whose studies demonstrated low speech scores in patients after TL. However, their overall QOL remained intact.

To further characterize patients’ health-related QOL outcomes, we stratified the mean domain scores based on certain pretreatment factors to determine if there was any correlation. All of our patients used an indwelling Bloom-Singer voice prosthesis. Patients who had primary TEP placement had statistically significant better eating outcomes and overall functional outcomes compared with patients who had secondary TEP placement. In addition, scores on speech, social disruption attitude, and overall function were higher for patients receiving primary TEP placement. Chone et al22 and Kao et al23 also found better outcomes in patients with primary TEP placement. These outcomes may be a result of small sample sizes of patients with secondary TEP placement. It is also possible that patients who receive primary TEP prostheses are more motivated to learn how to speak with the prosthesis because they have no other means to vocally communicate. In contrast, patients who receive secondary TEP prostheses may be less motivated to use this form of speech, as the delay before placement allows many patients the opportunity to acquire other forms of vocal communication (eg, esophageal speech).

There was notably better QOL in patients younger than 65 years compared with patients 65 years or younger, which was an unexpected finding. Younger patients may have better pretreatment functional status. They are more likely than their older counterparts to be active before their surgery. When subjected to an extensive surgical procedure, their baseline functional status drastically declines. As a result, their perception of QOL dramatically decreases. In contrast, older patients frequently have a more sedentary preoperative lifestyle. There may be little change in their baseline functional status after surgery. Therefore, their perception of their QOL may not be as negatively affected. To fully evaluate this hypothesis, future studies should include preoperative and postoperative measurement of activities of daily living and of QOL.

Patients with more than 2 comorbidities had worse functional outcomes. This finding is important because it suggests that the lower scores are not solely from the surgery but rather are a collective effect of the previous comorbidities and the surgery. Arriaga et al24 and Terrell et al25 determined that the presence of multiple comorbidities was a clinical predictor of worse QOL.

To our surprise, previous RT did not have an effect on long-term QOL outcomes. This was most likely due to the fact that patients without prior RT eventually undergo RT after surgery. Therefore, all patients had RT at one time or another. There was a significant difference in the eating domain between the patients who had chemoradiation therapy before surgery and those who did not. Previous chemoradiation therapy correlated with poorer eating status and was associated with worse outcomes in all of the domains. This finding is in agreement with a previous study by LoTempio et al3 in which patients who had chemoradiation therapy experienced increased difficulty in swallowing and chewing and exhibited greater pain.

This study provides insight into which pretreatment factors affect survival in patients with advanced-stage laryngeal cancer who have undergone TL. Patients with advanced-stage cancer (T4), recurrent tumor, N2 or greater neck disease, more than 2 comorbidities, or a single cardiovascular comorbidity are more likely to have a significant decrease in their 5-year survival.

CONCLUSIONS

©2007 American Medical Association. All rights reserved.
This study also reaffirms the idea that patients who have undergone TL can have functional lives and maintain good overall QOL. Predictors of good QOL include age older than 65 years at diagnosis, presence of no more than 2 comorbidities, no history of previous chemoradiation therapy, and primary TEP placement.

Submitted for Publication: June 7, 2006; final revision received November 27, 2006; accepted December 8, 2006.

Correspondence: Guy J. Petruzzelli, MD, PhD, MBA, Department of Otolaryngology, Rush University Medical Center, 1725 W Harrison, Suite 218, Chicago, IL 60612 (Guy_Petruzzelli@rush.edu).

Author Contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Woodward, Oplatek, and Petruzzelli. Acquisition of data: Woodward, Oplatek, and Petruzzelli. Analysis and interpretation of data: Woodward, Oplatek, and Petruzzelli. Drafting of the manuscript: Woodward, Oplatek, and Petruzzelli. Critical revision of the manuscript for important intellectual content: Woodward, Oplatek, and Petruzzelli. Administrative, technical, and material support: Woodward, Oplatek, and Petruzzelli. Study supervision: Petruzzelli.

Financial Disclosure: None reported.

REFERENCES