Clinical Predictors of Quality of Life in Patients With Head and Neck Cancer

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Objective: To identify clinical predictors of quality of life (QoL) in a head and neck cancer patient population.

Design, Patients, and Setting: A convenience sample of 570 patients with upper aerodigestive tract cancers were surveyed at a tertiary care oncology clinic and Veterans Affairs otolaryngology clinic.

Interventions: A self-administered health survey was constructed to collect demographic, health, smoking, alcohol, depression symptom, and QoL information. Tumor site and tumor stage, clinical, and treatment data were abstracted from the patient medical records.

Main Outcome Measures: Quality of life was assessed using the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36) and the Head and Neck QoL (HNQoL) instrument.

Results: Of the 570 eligible respondents, the presence of a feeding tube had the most negative impact on QoL, with significant decrements in 6 of the 8 SF-36 scales and all 4 HNQoL scales (P<.01). In descending order of severity, medical comorbid conditions, presence of a tracheotomy tube, chemotherapy, and neck dissection were also associated with significant (P<.05) decrements in QoL domains. Patients who took the survey more than 1 year after diagnosis had improved QoL in 7 of 12 domains. Hospital site, age, education level, sex, race, and marital status were also significant predictors of QoL.

Conclusion: There are at least 13 demographic and clinical characteristics that are significant predictors of QoL in patients with head and neck cancer, which should be considered when treating patients and conducting QoL studies in the future.

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Research on treatment decision making has suggested that patients frequently make treatment decisions based on probability of survival. However, when 2 different treatment modalities have similar survival rates, quality of life (QoL) factors are important considerations for patients. In head and neck cancer treatment, QoL issues and assessment of QoL outcomes are especially important for patients and their caregivers because of the potential impact on important functions such as speech, swallowing, and breathing, as well as cosmesis and communication.

The body of research on QoL issues in head and neck cancer is growing rapidly. Multiple studies have evaluated predictors of QoL in a cross section of patients who have primary cancers at a particular site or treated by a particular modality or modalities. Very few of the clinical studies that include QoL measures include more than 100 patients—probably related to the burden of collecting such large quantities of data. Unfortunately, small sample sizes make QoL analysis difficult: the numerous potential predictors of QoL necessitate larger sample sizes to control for all of the potential confounding variables.

Typically, researchers have studied a variety of predictors of QoL, including tumor characteristics, clinical characteristics, treatments, health behaviors (eg, alcohol use or smoking), and demographics. Tumor characteristics such as site and stage, as well as surgical, radiotherapeutic, and chemotherapy treatment modalities and number of modalities, are associated with QoL. Notably, primary site surgery has been shown to affect speech, swallowing, and cosmesis, and radiation therapy predominantly affects swallowing and taste. Multiple authors have noted that neck dissection is a predictor of physical functioning and bodily pain.
ity scales have been shown to predict survival\textsuperscript{13-17} as well as QoL, but few studies include comorbidity in multivariate analyses for predicting QoL.\textsuperscript{18} Many treatment studies have been hampered by small sample sizes and therefore limited ability to adequately analyze the potential breadth of predictor variables.

Health behaviors such as smoking and alcohol use (the major risk factors for head and neck cancer) have been shown to affect survival,\textsuperscript{15,17,19} but may affect overall QoL as well.\textsuperscript{20} These behaviors also vary by sex, with women smoking and using alcohol at lower rates than men.\textsuperscript{21} In patients with head and neck cancer, the impact of smoking and alcohol use on QoL has received little attention. Does one need to control for alcohol in QoL studies? In our pilot data, we found that alcohol use was not associated with QoL, but smoking was negatively associated with 5 scales of the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36).\textsuperscript{22} Allison\textsuperscript{12} presented data that alcohol use was associated with improvements in QoL for patients with head and neck cancer. Not surprisingly, numerous studies have shown that depression negatively affects QoL in head and neck cancer patients,\textsuperscript{6,25,26} but few, if any, studies have included enough patients to look at depression in the context of all of the demographic, tumor, clinical, behavioral, and treatment factors, which may confound depression as a predictor of QoL.

Demographic analysis has shown that among patients with head and neck cancer, women have lower QoL scores compared with men.\textsuperscript{6,25,26} Allison et al\textsuperscript{2} demonstrated that unemployment, older age, and female sex predicted worse global QoL rating, and Fang et al\textsuperscript{18} reported that patients with higher economic status, with higher educational levels, who were employed, or with-\textsuperscript{21}out comorbidity tended to enjoy better QoL. Quality of life and survival rates are also better for married persons and those not living alone compared with unmarried persons and those living alone.\textsuperscript{27}

In the present study, we have collected a large number of clinical variables, health behavior variables, and demographic variables as part of a larger intervention study of QoL in patients with head and neck cancer. The goal of this subproject was to elucidate those clinical variables that might be important predictors of QoL in a general head and neck cancer population, while controlling for mental health, health behavior, and demographic variables.

\section*{METHODS}

\section*{DESIGN}

A research assistant distributed a self-administered questionnaire on smoking, alcohol, depression, and QoL to patients with head and neck cancer while they were waiting to be seen for their scheduled otolaryngology clinic appointment. The research assistant helped patients in completing the questionnaire as needed. Institutional review board approval was obtained prior to conducting this study.

\section*{SAMPLE}

The research assistant originally approached 998 patients for participation in this study, and 197 (20\%) refused the survey and 106 (11\%) never returned a completed survey. Of the 696 patients who were screened, 108 (16\%) were ineligible because they did not have cancer or had other cancers not included in this study, and another 18 patients were dropped from this analysis owing to incomplete data. The results presented herein are from the remaining 570 subjects. Inclusion criteria were patients with head and neck cancer who, from the time of diagnosis and any time thereafter, were (1) not pregnant; (2) at least 18 years of age; (3) English speaking; and (4) free from severe unstable psychiatric/mental conditions such as suicidal ideation, acute psychosis, or dementia.

Respondents were recruited from both a Veterans Affairs (VA) and university hospital. While patients from the university hospital may be more representative of the general population of head and neck cancer patients, VA patients are at greater risk for these problems.\textsuperscript{28,29} Hence, inclusion of patients from both the VA and university hospital provided a diverse sample of head and neck cancer patients.

\section*{MEASURES}

A self-administered health survey was constructed to collect demographic, health, smoking, alcohol, depression symptom, and QoL information. When possible, previously validated questions and instruments (described in the following subsections) were used. Tumor site and tumor stage were abstracted from the patient medical records, as well as information on the forms of treatment the patient had received at the time of the survey.

\section*{Clinical Measures}

Health measures were abstracted from the patient medical records and included tumor site, tumor stage, date of diagnosis, types and dates of surgery, and whether the patient had undergone any of the following procedures at the time of the survey: laryngectomy, radiation therapy, and chemotherapy. Information on whether the patient had a feeding tube or tracheotomy tube at the time of the survey was also recorded. Other studies have indicated that laryngeal patients do best,\textsuperscript{33} therefore tumor site was segregated into 3 groups: (1) oropharynx or hypopharynx; (2) oral cavity or other; and (3) larynx.

Stage of the tumor was dichotomized based on severity into stage 0, I, and II vs stage III and IV. A person’s QoL may be affected by the length of time between the initial diagnosis and the time the survey was taken and whether they are still receiving treatment.\textsuperscript{6,34,35} Hence, we controlled for time in the analysis by comparing recent diagnoses (0-1 month) and distant diagnoses (>1 year) with 1 month to 1 year since diagnosis (most likely to be receiving treatment).

\section*{Health Behavior Measures}

To control for health behaviors, the survey had questions about smoking, alcohol intake, and the presence of depression symptoms. The survey incorporated several previously validated instruments, including the Fagerstrom Test for Nicotine Dependence (FTND),\textsuperscript{36} the Alcohol Use Disorder Identification Test (AUDIT),\textsuperscript{37} and the Geriatric Depression Scale–Short Form (GDS-SF).\textsuperscript{38,39} For this study, patients who (1) smoked in the last 6 months were considered to have a smoking problem; (2) had an AUDIT score of 8 or more and had drunk alcohol within the past 6 months were considered to have an alcohol problem; and (3) had a GDS-SF score of 4 or more were considered to have depression symptoms.

\section*{Demographic Measures}

Demographic measures consisted of age, sex, race, marital status, education, employment, hospital type (VA or university),
and miles traveled to the hospital. Since there were so few African American (n=29) and other race respondents (n=13) compared with whites (n=521), race was classified into white and nonwhite. Marital status was grouped into currently married; divorced, separated, or never married; and widowed. Education was classified into 3 groups: high school diploma or less; some college; and bachelor’s degree or higher. Respondents were also asked to indicate if they had any of the following comorbid conditions: other cancer, lung disease, heart disease, stroke, psychiatric problems, diabetes, or arthritis. These self-reported conditions were then totaled and classified into 3 groups including 0, 1, or more than 1 comorbid condition.

QoL Measures

Quality of life was assessed using the SF-36.40 The SF-36, a general health status measure, is well validated and commonly used to measure physical, social, role, and emotional functioning. Low scores on the 8 subscales of the SF-36 indicate a poorer QoL.

In addition to the SF-36, which measures overall QoL, disease-specific instruments are often used to capture compromises in QoL brought about by specific conditions. The Head and Neck Quality of Life (HNQoL) instrument41 is a multiple-domain, disease-specific QOL instrument for head and neck cancer patients. It is a concise, reliable, and comprehensive instrument for the assessment of head and neck cancer-specific QoL. The HNQoL instrument includes 20 items scored on a 5-point rating scale covering 4 domains: (1) eating and swallowing; (2) communication; (3) head and neck pain; and (4) emotional well-being.

DATA ANALYSIS

The data were double entered into a Microsoft Access (Microsoft Inc, Redmond, Wash) database and then were analyzed using SAS statistical software (SAS Institute Inc, Cary, NC). Since all of the respondents did not answer all of the questions, the sample size may vary for different results. P<.05 was considered significant.

Descriptive statistics (means and frequencies) were computed for all demographic and health characteristics; smoking, alcohol, and depression symptoms; and QoL scores (Table 1 and Table 2). The x² test was used for categorical variables, and the t test was used for interval level variables. Linear regression tests were conducted to determine the influence on the SF-36 and HNQoL instruments of the independent variables thought to be most influential to QoL.

RESULTS

DESCRIPTION OF THE SAMPLE

The clinical characteristics of the sample are summarized in Table 1, and the demographics and health behaviors are summarized in Table 2. Although smoking and alcohol are significant risk factors for head and neck cancer,39,42 37% of these head and neck cancer patients had smoked within the past 6 months. Thirteen percent were considered to have a drinking problem (drinking within the past 6 months and an AUDIT score ≥8). Depression symptoms were a considerable problem for this population, with 44% screening positive (a GDS-SF score of ≥4).

Twelve regression analyses were conducted using the 8 SF-36 and 4 HNQoL scales as the dependent variables (Table 3). All of the variables in Tables 1 and 2 were included in the analyses to control for any confounding effects. Of the health characteristics, having a current feeding tube had the most impact on the QoL scores in these multivariate analyses. The presence of a feeding tube had a significant negative association with 6 of the 8 SF-36 scales and all 4 HNQoL scales (P<.01) and also had a significant (P<.05) negative association with the physical composite summary score of the SF-36 but not the mental composite summary score (not included in Tables 1 and 2). Those who self-reported having 2 or more comorbid conditions had a significant (P<.05) lower score on 7 of the 8 SF-36 scales and on the pain HNQoL scale compared with those with no comorbid conditions. Having only 1 self-reported comorbid condition was not significantly different from having none in the multivariate analysis. Presence of a tracheotomy tube also showed strong significant negative associations with the role-physical and social functioning subscales of the SF-36 and with the speech and emotion HNQoL scales (P<.05). Cancer site showed significant (P<.05) associations with the HNQoL scales. Patients with oropharynx or hypopharynx and oral cavity or other cancers had worse scores on the HNQoL eating scale compared with patients with cancers of the larynx (P<.01). However, the association went in the other di-

Table 1. Clinical Characteristics of Patients With Head and Neck Cancer*

<table>
<thead>
<tr>
<th>Tumor site (n = 551)</th>
<th>Oropharynx</th>
<th>Hypopharynx</th>
<th>Larynx</th>
<th>Oral cavity</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation treatment (n = 553)</td>
<td>162 (29)</td>
<td>30 (5)</td>
<td>163 (30)</td>
<td>135 (25)</td>
<td>61 (11)</td>
</tr>
<tr>
<td>Feeding tube at time of survey (n = 553)</td>
<td>70 (13)</td>
<td>92 (18)</td>
<td>131 (25)</td>
<td>231 (44)</td>
<td></td>
</tr>
<tr>
<td>Tracheotomy at time of survey (n = 552)</td>
<td>23 (4)</td>
<td>65 (12)</td>
<td>320 (58)</td>
<td>61 (11)</td>
<td></td>
</tr>
<tr>
<td>Primary site surgery (excluding laryngectomy) (n = 553)</td>
<td>254 (46)</td>
<td>239 (43)</td>
<td>348 (63)</td>
<td>113 (20)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are number (percentage) of patients (N = 570).
Table 2. Demographics and Health Behaviors of Patients With Head and Neck Cancer*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range), y</td>
<td>59 (27-88)</td>
</tr>
<tr>
<td>Hospital site (N = 570)</td>
<td></td>
</tr>
<tr>
<td>University of Michigan</td>
<td>465 (82)</td>
</tr>
<tr>
<td>Ann Arbor Veterans Affairs Hospital</td>
<td>105 (18)</td>
</tr>
<tr>
<td>Sex (N = 570)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>443 (78)</td>
</tr>
<tr>
<td>Female</td>
<td>127 (22)</td>
</tr>
<tr>
<td>Race (n = 563)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>521 (92)</td>
</tr>
<tr>
<td>Nonwhite (all others)</td>
<td>42 (8)</td>
</tr>
<tr>
<td>Marital status (n = 562)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>352 (62)</td>
</tr>
<tr>
<td>Separated/divorced/never married</td>
<td>161 (29)</td>
</tr>
<tr>
<td>Widowed</td>
<td>49 (9)</td>
</tr>
<tr>
<td>Educational level (n = 561)</td>
<td></td>
</tr>
<tr>
<td>≤High school diploma</td>
<td>299 (53)</td>
</tr>
<tr>
<td>&lt;4 y of college</td>
<td>168 (30)</td>
</tr>
<tr>
<td>≥Bachelor's degree</td>
<td>94 (17)</td>
</tr>
<tr>
<td>Smoking problem† (n = 560)</td>
<td></td>
</tr>
<tr>
<td>Alcohol use disorder test score ≥8</td>
<td></td>
</tr>
<tr>
<td>Depression problem§ (n = 549)</td>
<td></td>
</tr>
<tr>
<td>Smoking problem† (n = 560)</td>
<td></td>
</tr>
<tr>
<td>Alcohol use disorder test score ≥8</td>
<td></td>
</tr>
<tr>
<td>Depression problem§ (n = 549)</td>
<td>244 (44)</td>
</tr>
</tbody>
</table>

*aData are number (percentage) of patients (N = 570) unless otherwise specified.
†Smoked in the past 6 months.
‡Alcohol Use Disorder Identification Test score ≥8.
§Geriatric Depression Scale ≥4.

rection for the speech scale: patients with oropharynx or hypopharynx and oral cavity or other cancers had better speech scores on the HNQoL scale compared with patients with cancer of the larynx (P<.01). Cancer stage was not significantly associated with any of the QoL scales.

Certain forms of treatment showed significant associations with the QoL scales. Total laryngectomy had a significant negative association with the social functioning scale of the SF-36 and with the speech scale on the HNQoL (P<.05). Having a neck dissection (either left or right) was associated with lower physical functioning on the SF-36 (P<.05). Previous chemotherapy for head and neck cancer had a negative association with the physical functioning, role-physical, bodily pain, and vitality scales of the SF-36 (P<.05). Radiation therapy was negatively associated with only the eating scale of the HNQoL (P<.01). Undergoing surgery at the primary site was associated with only the speech HNQoL scale (P<.05). The time since the subject’s most recent diagnosis also had an affect on QoL scores. Those who took the survey more than a year after their most recent diagnosis had a significant positive association on the role-physical, bodily pain, and social functioning scales of the SF-36 compared with those who were between 1 month and 1 year of their diagnosis. There was also a significant (P<.05) positive association with the speech, emotion, and pain scales of the HNQoL. Those who took the survey less than 1 month after being diagnosed had a significant (P<.05) negative association with only the pain scale of the HNQoL compared with those taking the survey within 1 month to 1 year of their diagnosis.

In this study, 2 clinical variables (feeding tube status and comorbid conditions) were found to be very strong and significant predictors of QoL scores. The most frequent predictor of QoL among the clinical variables we collected was the presence of a feeding tube. The presence of a feeding tube was associated with statistically lower scores on 10 of the 12 collective domains included in the SF-36 and HNQoL instruments and was much more important than the presence of a tracheotomy tube, which predicted a decrement in only 4 of the QoL domains we measured, or laryngectomy, which was associated with decrements in QoL scores in only 2 domains.

Physical functioning on the SF-36 (defined as limitations in patients’ ability to perform concrete activities) was 16.3 points lower in those patients with feeding tubes after controlling for demographic, behavior, disease, and treatment variables. Scores on the SF-36 related to problems with work or other daily activities as a result of physical health (role-physical) were a dramatic 29.6 points lower for patients with feeding tubes than for those without, reflecting the degree of problems with activities of daily living that these patients experience. Our clinical impression is that despite our best efforts to support patients nutritionally with tube feedings, patients who require feeding tubes are nutritionally compromised, and hence they are weak. It is also possible that patients with feeding tubes may be limited physically because they cannot recover nutritionally owing to problems, adverse effects, and complications that are commonly associated with cancer, cancer treatment, and/or enteral feeding. This theory is supported by the work of Callahan et al., who found that feeding tubes were commonly associated with complications including vomiting, diarrhea, constipation, and nausea as well as aspiration symptoms, obstructed tubes, redness, irritation, infections, bleeding, and leakage around the percutaneous endoscopic gastronomy site. These problems and complaints related to feeding tubes may explain the lower SF-36 bodily pain and HNQoL pain scores for patients with feeding tubes in the present study as well as the low physical functioning, role-physical, and vitality scores found in the multivariate analysis.

It was also notable that patients with feeding tubes had substantially lower social functioning scores on the SF-36 and lower emotion scores on the HNQoL. The SF-36 social functioning domain measures the extent and frequency of interference with social activities due to physical and emotional problems. The emotion domain of the HNQoL queries patients on embarrassment about one’s condition, concerns about appearance, and frustration with one’s condition. Our impression is that the presence of the feeding tube and the process of tube feeding is a constant reminder of their disease in spite of completion of therapy and/or eradication of the cancer. Moreover, these patients are less likely to enjoy the so-
cial aspects of eating (going out to dinner) given their dysphagia and feeding tube. This may explain much of the decrements in social functioning and emotion domains for patients with feeding tubes.

Comorbid Conditions

It is not surprising that the number of comorbid conditions was the second greatest predictor of decreased QoL and was associated with 8 of the QoL scales. In the present study, 2 or more self-reported medical comorbid conditions predicted a moderate 4- to 12-point decrement in QoL scores for 7 domains of the SF-36 as well as an 8-point decrement in the pain domain of the HNQoL. As one might expect, these decrements were noted more so in the physical domains than in the emotional or mental health domains of the SF-36. Comorbid conditions did not affect the eating, speech, or emotion domains of the more disease-specific HNQoL instrument.

Multiple authors have demonstrated that comorbidity among patients with head and neck cancer is an important predictor of survival. We have demonstrated that comorbidity is an important predictor of QoL that should be considered as an independent variable in future QoL studies. This study also demonstrates that it is possible to assess comorbidity in head and neck cancer patients by questionnaire, rather than by medical chart review, which is far more commonly used but also much more labor intensive and costly. However, whether questionnaire or medical chart review comorbidity indexes are more sensitive or valid cannot be addressed by this study. Further research on patient-reported comorbid conditions may be warranted.

MODERATE CLINICAL PREDICTOR VARIABLES OF QoL

Four clinical variables were found to be predictors of decreased QoL in a moderate number (4-6) of the QoL scales: time since diagnosis, cancer site, presence of a tracheotomy tube, and chemotherapy.

Time Since Diagnosis

Not surprisingly, time since diagnosis was found to positively influence 6 of the 12 QoL scales. Patients who took the survey more than 12 months after diagnosis had better QoL for the SF-36 role-physical, bodily pain, and social functioning domains, as well as the speech, emotion, and pain domains of the HNQoL. Our study confirms findings from other studies regarding time since treatment as predictors of health-related QoL and validates the usefulness of the HNQoL and SF-36 as sensitive tools for the measurement of the changes known to occur over time in the head and neck cancer patient populations. Other authors have demonstrated that this, to a great degree, represents resolution of tumor-related symptoms as well as treatment-related adverse effects, but there may also be some resetting of patient expectations as they become accustomed to treatment sequelae. Patients with chronic illnesses or disabilities often adapt physically and emotionally to their condition. In addition, this association may be related to survivorship effect (ie, the healthier patient surviving with better QoL).

<table>
<thead>
<tr>
<th>Clinical Predictors</th>
<th>SF-36 QoL</th>
<th>HNQoL Scales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer site (vs larynx)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx/hypopharynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity/other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer stage (III/IV vs 0-II)</td>
<td>-21.6</td>
<td>-16.3</td>
</tr>
<tr>
<td>Current tracheotomy</td>
<td>-16.3</td>
<td>-29.6</td>
</tr>
<tr>
<td>Current feeding tube</td>
<td>-15.4</td>
<td>-8.5</td>
</tr>
<tr>
<td>Total laryngectomy</td>
<td>-8.9</td>
<td>-8.9</td>
</tr>
<tr>
<td>Surgery at primary site (excluding laryngectomy)</td>
<td>-10.1</td>
<td>-10.1</td>
</tr>
<tr>
<td>Neck dissection</td>
<td>-10.6</td>
<td>-10.6</td>
</tr>
<tr>
<td>Radiation</td>
<td>-15.1</td>
<td>-15.1</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>-9.2</td>
<td>-9.2</td>
</tr>
<tr>
<td>No. of comorbidity conditions (vs 0)</td>
<td>-13.3</td>
<td>-9.2</td>
</tr>
<tr>
<td>1</td>
<td>(2.1 NS)</td>
<td>(1.9 NS)</td>
</tr>
<tr>
<td>≥2</td>
<td>(−0.3 NS)</td>
<td>(−4.1 NS)</td>
</tr>
<tr>
<td>Time since diagnosis (1-12 mo)</td>
<td>-12.4</td>
<td>(−4.3 NS)</td>
</tr>
<tr>
<td>&lt;1 mo</td>
<td>-10.6</td>
<td>(−0.8 NS)</td>
</tr>
<tr>
<td>≥1 y</td>
<td>−9.1</td>
<td>(−1.0 NS)</td>
</tr>
<tr>
<td></td>
<td>6.8</td>
<td>(−3.9)</td>
</tr>
<tr>
<td></td>
<td>6.6</td>
<td>(−8.3)</td>
</tr>
<tr>
<td></td>
<td>5.8</td>
<td>(−13.3)</td>
</tr>
<tr>
<td></td>
<td>5.7</td>
<td>(−11.9)</td>
</tr>
</tbody>
</table>

Abbreviations: HNQoL, Head and Neck Quality of Life; NS, individual predictor not significant; QoL, quality of life; SF-36, Medical Outcomes Study Short-Form 36-Item Health Survey.

*Significant (P<.05) parameter estimates for clinical variables on SF-36 and HNQoL scales. Regressions also controlled for various health behavior (smoking, alcohol, and depression) and demographic characteristics (data not shown).
Tracheotomy

Having a tracheotomy tube also decreased QoL on 4 of the scales including the speech and emotional domains of the HNQoL instrument. While this was expected, it was not nearly as predictive of decreased QoL as was the presence of a feeding tube previously mentioned. Clinicians typically feel that tracheotomy affects QoL, but this article also quantifies the effect of tracheotomy by using standardized QoL instruments. Our clinical impression at the onset of the study was that patients with tracheotomy tubes would be more likely to have depression symptoms. In fact, although a tracheotomy tube was associated with markedly more complaints related to limitations in social activities (16.4 decrease on the social functioning scale), there was no relationship between tracheotomy and levels of anxiety or depression as measured by the mental health domain of the SF-36 on multivariate analysis. Similarly, our impression prior to the study was that patients with tracheotomy tubes might be more physically limited by the tracheotomy tube. Although patients with a tracheotomy tube were more likely to be limited by physical problems in their usual daily activities, there was no association between presence of a tracheotomy tube and scores on the physical functioning domain, which measures ability to perform concrete physical activities (ie, lifting or carrying). In other words, the tracheotomy tube likely interfered with work or other daily activities, but was not associated with problems with actual physical activity. This is in contrast to the feeding tube, which was associated with decrements in physical activity (−16.3 points on the physical functioning scale) as well as limitations in work and other activities due to physical problems (−29.6 points on the role-physical scale).

Chemotherapy and Radiation Therapy

While it is not surprising that those who have undergone chemotherapy had decreased QoL on 4 of the 8 SF-36 scales, one might expect that the adverse effects of chemotherapy would influence an even greater number of the QoL scales. Notably, chemotherapy was not associated with worse scores in the more emotional domains of the SF-36 (social functioning, role-emo, and mental health domains) but primary predicted worse physical scores (physical functioning, role-physical, and bodily pain scales). In contrast to chemotherapy, radiation therapy only adversely affected the eating domain scores of the HNQoL (−13.0 points; P < .01), presumably from the xerostomia and other effects of radiation on tissues. Further work on assessing the impact of xerostomia on QoL is currently in progress. This would confirm our clinical observations as well as our previous work on the health impact of treatment modalities. That is, each additional treatment modality extracts its own toll on physical health and QoL for patients with head and neck cancer.

Cancer Site and Stage

Patients with larynx cancer had better eating scores and worse speech scores compared with patients with cancers at all other head and neck cancer sites, but they otherwise had similar general health status scores on the SF-36 and HNQoL instruments. Better speech scores do not seem surprising given that patients with oropharynx, hypopharynx, or oral cavity cancer have intact larynges (better voice). This corroborates our previous work that showed that patients with laryngeal cancer have better swallowing and worse speech scores compared with patients with cancers at other head and neck sites. It is possible that the lower eating scores in the oropharynx, hypopharynx, or oral cavity cancer group may be related to dysphagia, which laryngeal cancer patients may not experience as much since patients with successful laryngeal preservation and even those after laryngectomy do not typically complain as much about dysphagia. Because most patients with laryngeal cancer at our study centers have either organ preservation therapy or laryngectomy, swallowing is often fairly well preserved relative to patients with oral and pharyngeal cancers who often have surgery and/or receive radiation therapy, both of which have the potential to substantially affect swallowing function with cancers of the pharynx.

Unlike cancer site, cancer stage was not associated with any of the QoL scales, corroborating a similar finding of Hammerlid and Taft. While one might think that those persons with late stage cancer would have decreased QoL, many of our patients with advanced cancers (stage III and IV) are treated with surgery-sparing, chemoradiation protocols, which may potentially preserve function and QoL. In addition, QoL decrements that one may expect with more advanced cancer stages may be, to a great degree, related to cancer treatment and number of treatment modalities rather than cancer stage, thereby making stage a less significant predictor of QoL in multivariate analyses such as the present study.

WEAKER PREDICTOR VARIABLES OF QoL

Several other clinical factors deserve mention as significant predictors of QoL on only a few of the QoL scales. These factors include laryngectomy, neck dissection, and primary site surgery.

Laryngectomy

First, laryngectomy status was an independent predictor of a 10-point lower social functioning score on the SF-36 and 11.5-point lower HNQoL speech score. Of note, the decrements for social functioning for laryngectomy patients (−10.1) were of a lesser magnitude than those associated with feeding tubes (−18.1) or tracheotomy tubes (−16.1). Similarly, laryngectomy patients had less of a decrement in HNQoL speech scores than that associated with presence of a feeding tube (−24.2) or tracheotomy tube (−18.9). We expected that laryngectomy might have been associated with even larger decrements in speech domains score, and we surmise that larger decrements were not seen because of the following 3 factors: (1) excellent rehabilitation of patients with a laryngeal speech, (2) adjustment of patients’ expectations and “bother” as they become experienced with a laryngeal speech production, and (3) the fact that many (nonlar-
yneectomy) patients with head and neck cancer have difficulties with speech production as well.

**Neck Dissection**

Neck dissection (any type) was associated with a 10.6-point lower score on the SF-36 physical functioning domain, corroborating the work of many authors on the impact of neck dissection on health status and QoL.

In this study, we did not perform analysis for nerve-sparing type neck dissections vs radical neck dissections, the latter of which has been demonstrated to be more debilitating in terms of function and QoL. While these data on the debilitation associated with neck dissection are not new, it does shed light on the health impact of neck dissection relative to other clinical factors that affect health status or QoL. These data demonstrate that those patients with more medical comorbid conditions or a feeding tube have greater decrements in physical functioning compared with those patients who underwent neck dissection. However, neck dissection was associated with worse physical functioning scores (−10.6 points) compared with chemotherapy, which was associated with a 9.2 decrement in physical functioning scores (but also lower role-physical, bodily pain, and vitality scores on the SF-36). Future studies that investigate general health status in patients with head and neck cancer should include neck dissection as an important variable, and the type of neck dissection (nerve sparing vs nerve preserving) or postoperative nerve function should be collected and analyzed, if possible.

**Primary Site Surgery**

Owing to the large sample size and multivariate analysis in this study, the relative impact of primary site surgery could be assessed while controlling for many other important clinical variables. Primary surgery was associated with a decrement of QoL (−7.6 points) only in the speech domain of the HNQoL and none of the other disease-specific or SF-36 health scales. It should be noted that laryngec- tomy was analyzed separately from other primary site surgical procedures and affected 2 domains (social functioning on the SF-36 and speech on the HNQoL). It is interesting that the number of QoL domains affected, and in many cases the magnitude of decrements in scores, were sol less for primary site surgery than for radiation treatment, chemotherapy treatment, laryngec- tomy, neck dissection, or tracheotomy or feeding tube status. Once demographic, clinical, treatment, and health behaviors have been controlled for, primary site surgery had less of a predictive effect on QoL than one might expect.

These data would suggest that primary site surgery, by itself, is associated with only moderate decrements in speech scores, but no significant differences in any of the other QoL domains. Patients who require postoperative chemotherapy, radiation therapy, feeding tube, or tracheotomy tube (ie, for airway security or difficulty with secretions) are likely to have decrements in other domains of general health or disease-specific QoL scores. Clearly, each treatment modality is associated with its own potential for adverse effects that may alter health status and QoL.

As future research in cancer therapy is done, it will be important to recognize that minimizing the numbers of modalities of therapy is important to the functioning and well-being for our patients. These findings would support the necessity for ongoing research in biomarkers for “response to therapy.” If such biomarkers could predict successful treatment with only 1 treatment modality, then patients’ QoL could be preserved by eliminating the adverse effects of combined modality therapy.

In our population of head and neck cancer patients, no less than 13 different demographic and clinical characteristics were significant predictors of QoL. Of the clinical predictors, the presence of a feeding tube was a strong negative predictor across 10 of 12 domains of QoL studied, but multiple medical comorbid conditions, presence of a tracheotomy tube, previous chemotherapy, laryngec- tomy status, previous neck dissection, and radiation therapy (in descending order of severity) also had significant negative effects on a number of QoL scales. Future studies of QoL in the head and neck cancer population should attempt to have a large enough sample size to control for as many of these important clinical predictors as possible. More importantly, physicians should consider the impact of clinical treatments on QoL when discussing treatment options with patients. Future basic and clinical research that allows clinicians to select and successfully treat patients with fewer treatment modalities may offer hope of improving QoL for patients with head and neck cancer.

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