Pretreatment Health Behaviors Predict Survival Among Patients With Head and Neck Squamous Cell Carcinoma


ABSTRACT

Purpose
Our prior work has shown that the health behaviors of head and neck cancer patients are interrelated and are associated with quality of life; however, other than smoking, the relationship between health behaviors and survival is unclear.

Patients and Methods
A prospective cohort study was conducted to determine the relationship between five pretreatment health behaviors (smoking, alcohol, diet, physical activity, and sleep) and all-cause survival among 504 head and neck cancer patients.

Results
Smoking status was the strongest predictor of survival, with both current smokers (hazard ratio [HR] = 2.4; 95% CI, 1.3 to 4.4) and former smokers (HR = 2.0; 95% CI, 1.2 to 3.5) showing significant associations with poor survival. Problem drinking was associated with survival in the univariate analysis (HR = 1.4; 95% CI, 1.0 to 2.0) but lost significance when controlling for other factors. Low fruit intake was negatively associated with survival in the univariate analysis only (HR = 1.6; 95% CI, 1.1 to 2.1), whereas vegetable intake was not significant in either univariate or multivariate analyses. Although physical activity was associated with survival in the univariate analysis (HR = 0.95; 95% CI, 0.93 to 0.97), it was not significant in the multivariate model. Sleep was not significantly associated with survival in either univariate or multivariate analysis. Control variables that were also independently associated with survival in the multivariate analysis were age, education, tumor site, cancer stage, and surgical treatment.

Conclusion
Variation in selected pretreatment health behaviors (e.g., smoking, fruit intake, and physical activity) in this population is associated with variation in survival.


INTRODUCTION

Five-year survival rates for head and neck cancer have not changed in several decades and remain at approximately 60% depending on tumor site.\(^1,2\) Although new surgical, radiation, and chemotherapy regimens hold promise, healthy lifestyle behaviors may be instrumental in improving survival among head and neck cancer patients. A clearer understanding of the pretreatment health behaviors that are associated with improved survival may provide insight into the types of behavioral interventions needed among head and neck cancer patients.

Tobacco and alcohol use are well-known primary risk factors for developing head and neck cancer and have been shown to be associated with decreased quality-of-life scores\(^3,4\) and decreased survival.\(^5\) Diets high in fruits and vegetables are protective against most cancers of the head and neck,\(^6\) can affect the occurrence of second primary cancers,\(^7\) and are associated with reduced cancer mortality.\(^5\) Malnutrition,\(^8\) cachexia,\(^9\) and weight loss\(^10\) are poor prognostic indicators for head and neck cancer patients. There is also evidence that a sedentary lifestyle may promote certain types of cancer, such as colon or breast\(^11,12\); however, the association with physical activity and head and neck cancer is less clear. Sleep disturbances are common in head and neck cancer patients, and although there is no evidence of causality, associations have been drawn between amount of sleep and mortality.\(^12\)

In prior research, our team profiled the health behaviors of newly identified head and neck cancer patients at baseline and during the first year after diagnosis, but inadequate follow-up was available at that time to assess the associations between health behaviors and survival. Now, with longer follow-up, the present study was undertaken to determine...
whether five pretreatment health factors (including smoking, alcohol use, diet, exercise, and sleep) predict survival among head and neck cancer patients.

**RESULTS**

**Descriptive Statistics**

Descriptive characteristics of the sample are listed in Table 1. At the time of diagnosis, more than one quarter of patients were current smokers, whereas more than half were former smokers. More than one quarter of the patients screened positive for problem drinking. Approximately one third of patients ate fewer than four servings of fruit per month, and more than two-thirds ate less than one vegetable per day. The mean calorie intake was 2,351 calories per day, and the mean BMI was 26.7 kg/m². The mean physical activity score was 115, and the mean sleep score was 67. The 2-year death rate was 24.2% (SE = 1.99%). The median follow-up time was 999 days (range, 19 to 2,010 days).

**Univariate and Multivariate Analyses**

Univariate analyses showed that four of the five health behaviors (smoking status, alcohol problem, fruit intake, and physical activity, but not vegetable intake) were significantly associated with survival (Fig 1). Because there was no association between calories and BMI with survival in the univariate analyses, fruits and vegetables were chosen as the nutrition markers for the final multivariate analysis. In addition, several control variables (age, marital status, education, cancer stage, and comorbidities) were also associated with survival in the univariate analyses. The results of the univariate and multivariate Cox proportional hazards regression models are listed in Table 2.

All control variables were included in the multivariate analyses, regardless of the univariate results. Several of the control variables were associated with each other; however, the variance inflation factor was less than 2.5 for all variables in the multivariate regression, indicating that the multicollinearity was not severe. Hence, no variables were omitted from the multivariate model as a result of concerns about collinearity.
Of the health behaviors, pretreatment smoking status was the strongest predictor of survival, with both current smokers (hazard ratio [HR] 2.4; 95% CI, 1.3 to 4.4) and former smokers (HR 2.0; 95% CI, 1.2 to 3.5) showing significant associations with poor survival. Pretreatment problem drinking was associated with survival in the univariate analysis but not in the multivariate model. Low fruit intake was negatively associated with survival in only the univariate analysis, whereas vegetable intake was not significant in either the univariate or multivariate analysis. Physical activity was associated with survival in univariate analysis and was approaching significance in the multivariate model (HR 0.98; 95% CI, 0.95 to 1.00). However, sleep was not associated with survival in either the univariate or multivariate analyses. Control variables that were also independently associated with poor survival in the multivariate analysis were higher age, lower education, cancer site (oral cavity), and cancer stage. Those treated with surgery had improved survival. Sex, race, marital status, comorbidity score, and treatment with radiation or chemotherapy were not independently associated with survival in the multivariate analysis.

**DISCUSSION**

Because smoking is a major causative factor for head and neck cancer, it was not surprising that more than one quarter of patients smoked at diagnosis or that current smoking at diagnosis was the strongest predictor of survival among head and neck cancer patients in this population, as well as in previously reported studies.\(^{25,26}\) Approximately one in four head and neck cancer patients were smoking at the time of their diagnosis, and our prior work has shown that approximately half quit after diagnosis.\(^{27}\) Continued smoking may increase the risk of...
is associated with second primary tumors. Although approximately one quarter of patients were problem drinkers at diagnosis, unlike prior work has shown that continued drinking among this population may show a survival advantage for fruit and vegetable intake as assessed in this analysis, it is possible that patients may potentially have lead to xerostomia (dry mouth), which can make it more difficult to second primary cancers among head and neck cancer patients and decrease survival. Although it may be difficult to comprehend why a head and neck cancer patient would continue to smoke, nicotine dependence is an addiction, which is defined as “persistent compulsive use of a substance known by the user to be harmful.” Fortunately, efficacious cessation interventions, including medications (nicotine replacement therapy, bupropion, and varenicline), are available for head and neck cancer patients. Behavioral interventions, such as brief physician advice, nurse counseling, and 1-800-QUIT NOW telephone counseling, have been shown to increase quit rates.

Alcohol use, in conjunction with smoking, has been found to be a causative factor for head and neck cancer, and continued drinking is associated with second primary tumors. Although approximately one quarter of patients were problem drinkers at diagnosis, unlike other studies, pretreatment alcohol problem was not a predictor of survival in the multivariate analyses in this study. Similarly, our prior work has shown that continued drinking among this population is not associated with quality of life. It is important to note that smoking and alcohol use are highly interrelated, and problem drinkers may have a harder time quitting smoking. Moreover, alcohol use may complicate or interfere with adherence to treatment regimens. For some, treatment for alcohol use must first take place before smoking and alcohol use are highly interrelated, and problem drinkers may show a survival advantage for fruit and vegetable intake as assessed in this analysis, it is possible that patients may potentially have lead to xerostomia (dry mouth), which can make it more difficult to

ing cessation or other interventions can be accomplished. Unfortunately, for those who are highly alcohol dependent, inpatient detoxification programs may be needed. For others, referrals to outpatient and community-based programs such as Alcoholics Anonymous are effective strategies.

Surprisingly, before treatment, less than one third of patients reported eating more than five servings of fruit per week, whereas approximately one third reported eating less than four servings of fruit per month compared with an average of 1.5 servings per day for healthy adults. Similarly, less than one third of patients ate at least one vegetable per day, whereas one in five patients ate less than two servings of vegetables per week compared with an average of 3.7 servings per day for healthy adults. This is substantially less than the recommended nine servings of fruits and vegetables per day. Fruit intake predicted survival in the univariate analysis but did not predict survival in the multivariate analysis, whereas vegetable intake did not predict survival in either analysis. Longer follow-up may show a survival advantage for fruit and vegetable intake as shown in other studies.

Although fruit and vegetable intake after diagnosis was not assessed in this analysis, it is possible that patients may potentially have even worse dietary intake after treatment. For example, radiation can lead to xerostomia (dry mouth), which can make it more difficult to
eat particulate (rather than liquid) food items. Given poor pretreatment dietary intake, post-treatment difficulties with eating, and the potential prognostic value of fruits and vegetables, there may be a considerable and underemphasized need for nutrition counseling among head and neck cancer patients. Tailored, low-intensity nutrition interventions have been shown to increase fruit and vegetable consumption among head and neck cancer patients.42 Although pretreatment mean calorie intake was similar to the mean for the elderly population, both lower BMI and physical activity levels were found among this sample of head and neck cancer patients.49 Given the known negative effects of low physical activity during the often grueling treatment period, patients should conserve energy or push themselves to engage in physical activity once they are able.50

Table 2. Univariate and Multivariate Cox Proportional Hazards Models for Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Model</th>
<th>Multivariate Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status (v never smoker)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.43</td>
<td>1.41 to 4.20</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.95</td>
<td>1.16 to 3.27</td>
</tr>
<tr>
<td>Alcohol problem</td>
<td>1.41</td>
<td>1.02 to 1.96</td>
</tr>
<tr>
<td>PASE physical activity score (per 10 points)</td>
<td>0.95</td>
<td>0.93 to 0.97</td>
</tr>
<tr>
<td>MOS sleep scale (per 10 points)</td>
<td>0.94</td>
<td>0.88 to 1.02</td>
</tr>
<tr>
<td>Low fruit intake (none to 1-3 per month)</td>
<td>1.55</td>
<td>1.14 to 2.12</td>
</tr>
<tr>
<td>Low vegetable intake (none to 2-4 per week)</td>
<td>1.09</td>
<td>0.81 to 1.48</td>
</tr>
<tr>
<td>Age (in decades)</td>
<td>1.40</td>
<td>1.22 to 1.62</td>
</tr>
<tr>
<td>Female</td>
<td>0.72</td>
<td>0.48 to 1.07</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>1.25</td>
<td>0.80 to 1.96</td>
</tr>
<tr>
<td>Married</td>
<td>0.70</td>
<td>0.51 to 0.95</td>
</tr>
<tr>
<td>High school education or less</td>
<td>1.70</td>
<td>1.25 to 2.32</td>
</tr>
<tr>
<td>Cancer site (v oral cavity/sinus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Larynx cancer site</td>
<td>0.65</td>
<td>0.42 to 1.02</td>
</tr>
<tr>
<td>Pharynx cancer site</td>
<td>0.81</td>
<td>0.56 to 1.17</td>
</tr>
<tr>
<td>Stage</td>
<td>1.38</td>
<td>1.16 to 1.64</td>
</tr>
<tr>
<td>ACE-27 comorbidity score</td>
<td>1.39</td>
<td>1.18 to 1.63</td>
</tr>
<tr>
<td>Radiation</td>
<td>1.11</td>
<td>0.71 to 1.72</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1.04</td>
<td>0.76 to 1.43</td>
</tr>
<tr>
<td>Surgery</td>
<td>0.81</td>
<td>0.60 to 1.10</td>
</tr>
</tbody>
</table>

Hazard Ratio 95% CI P Hazard Ratio 95% CI P

NOTE. Of 504 patients, there were 166 events and 338 patients were censored. Abbreviations: PASE, Physical Activity Scale for the Elderly; MOS, Medical Outcomes Study; ACE-27, Adult Comorbidity Evaluation-27.

*Significant at P < .05.
shown in other studies, educational level (a marker for socioeconomic status) also predicted survival. Similar to other studies, oral cancer patients had poorer survival than did patients with pharyngeal or laryngeal cancers. Although human papillomavirus–positive tumors have been shown to be associated with improved survival, unfortunately, human papillomavirus status was not available for these analyses. As shown in multiple studies, those with higher cancer stage had poorer survival than those with lower cancer stage. Our work and that of others has shown that those with increased comorbidities had poorer survival; however, in this study, comorbidity scores were significantly associated with survival only in the univariate analysis. Similar to other studies that found an association between marital status (a marker for social support) and survival, being married in the present study was significantly associated with improved survival in the univariate analysis but was not an independent predictor in the multivariate model. Surgery was the only treatment variable associated with survival in the multivariate analysis, perhaps because, in many cases, those patients who receive surgery are the ones with the best prognosis (lower cancer stage and more localized disease). The lack of effects from radiation and chemotherapy is likely a result of the fact that there was little variability in treatment in that all patients were from tertiary care centers that provided standard of care treatment for their particular cancer site and stage. Interestingly, sex and race, which have been shown to predict survival in selected other studies of cancer patients, did not predict survival in this study.

To our knowledge, this study is the first to comprehensively assess the association of five pretreatment health behaviors and conventional prognostic factors with survival among head and neck cancer patients. Pretreatment health behaviors can identify those at risk for poor survival. Multicomponent behavioral interventions can be efficacious among head and neck cancer patients, and future research is needed to determine whether changes in the health behaviors after diagnosis can improve survival rates.

**Authors' Disclosure of Potential Conflicts of Interest**

The author(s) indicated no potential conflicts of interest.

**Conception and design:** Sonia A. Duffy, David L. Ronis, Karen E. Fowler, Stephen B. Gruber, Gregory T. Wolf, Jeffrey E. Terrell

**Financial support:** Sonia A. Duffy, Gregory T. Wolf

**Administrative support:** Karen E. Fowler, Gregory T. Wolf, Jeffrey E. Terrell

**Provision of study materials or patients:** Scott McLean, Gregory T. Wolf

**Collection and assembly of data:** Sonia A. Duffy, Karen E. Fowler, Gregory T. Wolf

**Data analysis and interpretation:** Sonia A. Duffy, David L. Ronis, Scott McLean, Karen E. Fowler, Stephen B. Gruber, Gregory T. Wolf, Jeffrey E. Terrell

**Manuscript writing:** Sonia A. Duffy, David L. Ronis, Karen E. Fowler, Stephen B. Gruber, Jeffrey E. Terrell

**Final approval of manuscript:** Sonia A. Duffy, Laura D. Ronis, Karen E. Fowler, Stephen B. Gruber, Gregory T. Wolf, Jeffrey E. Terrell

**Author Contributions**

Data analysis and interpretation: Gregory T. Wolf

Collection and assembly of data: Gregory T. Wolf

Conception and design: Sonia A. Duffy, David L. Ronis, Karen E. Fowler, Stephen B. Gruber, Gregory T. Wolf, Jeffrey E. Terrell

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Final approval of manuscript: Sonia A. Duffy, David L. Ronis, Scott McLean, Karen E. Fowler, Stephen B. Gruber, Gregory T. Wolf, Jeffrey E. Terrell

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