Predictors of Poor Sleep Quality Among Head and Neck Cancer Patients

Andrew G. Shuman, MD; Sonia A. Duffy, PhD, RN; David L. Ronis, PhD; Susan L. Garetz, MD; Scott A. McLean, MD, PhD; Karen E. Fowler, MPH; Jeffrey E. Terrell, MD

Objectives/Hypothesis: The objective of this study was to determine the predictors of sleep quality among head and neck cancer patients 1 year after diagnosis.

Study Design: This was a prospective, multisite cohort study of head and neck cancer patients (N = 457).

Methods: Patients were surveyed at baseline and 1 year after diagnosis. Chart audits were also conducted. The dependent variable was a self-assessed sleep score 1 year after diagnosis. The independent variables were a 1 year pain score, xerostomia, treatment received (radiation, chemotherapy, and/or surgery), presence of a feeding tube and/or tracheotomy, tumor site and stage, comorbidities, depression, smoking, problem drinking, age, and sex.

Results: Both baseline (67.1) and 1-year post-diagnosis (69.3) sleep scores were slightly lower than population means (72). Multivariate analyses showed that pain, xerostomia, depression, presence of a tracheotomy tube, comorbidities, and younger age were statistically significant predictors of poor sleep 1 year after diagnosis of head and neck cancer (P < .05). Smoking, problem drinking, and female sex were marginally significant (P < .09). Type of treatment (surgery, radiation and/or chemotherapy), primary tumor site, and cancer stage were not significantly associated with 1-year sleep scores.

Conclusions: Many factors adversely affecting sleep in head and neck cancer patients are potentially modifiable and appear to contribute to decreased quality of life. Strategies to reduce pain, xerostomia, depression, smoking, and problem drinking may be warranted, not only for their own inherent value, but also for improvement of sleep and the enhancement of quality of life.

Key Words: Head and neck cancer, sleep, pain, xerostomia.

Level of Evidence: 2c

Laryngoscope, 120:1166–1172, 2010

INTRODUCTION

Sleep disturbances are a common complaint in cancer patients with a reported incidence ranging from 30% to 75%.1 Sleep disturbances have been shown to decrease quality of life, decrease work productivity, increase utilization of health care resources, decrease mental health, and serve as a predictor of other complications in cancer patients.2–4 A recently published study by our team demonstrated that sleep disorders are common among head and neck cancer patients.5 However, the causes of sleep disturbances among head and neck cancer patients are unclear and have not been well studied. Head and neck cancer patients have a high prevalence of pain (70%) compared to other cancer sites (52%–60%), and pain is associated with insomnia.6 Pain is often correlated with depression among cancer patients, and the majority of depressed patients report insomnia.7,8 Depression is also correlated with nicotine and alcohol use, which are both common among head and neck cancer patients and have an adverse effect on sleep quality.9,10 Radiation therapy to treat head and neck tumors can also contribute to obstructive sleep apnea and xerostomia (dry mouth), the latter of which requires excessive drinking and urination during the night.11,12 Although there is reason to believe that head and neck cancer patients are at even greater risk for sleep disorders than other cancer patients secondary to high rates of pain, depression, nicotine and alcohol use, obstructive sleep apnea, surgical alterations or radiation
therapy, and xerostomia, the etiology and nature of these sleep disorders are largely anecdotal and unknown. Although efficacious interventions are available to treat sleep disorders, it is first necessary to determine the source of the sleep disorders prevalent in this population. Therefore, we hypothesized that specific clinical variables would affect sleep quality in head and neck patients in ways that might influence oncologic treatments themselves as well as the approach to medical management after the completion of therapy. Thus, the objective of this study was to determine the predictors of poor sleep among a large population of head and neck cancer patients.

MATERIALS AND METHODS

Design
The data were collected from a prospective cohort study of patients enrolled in the University of Michigan Head and Neck Cancer Specialized Programs of Research Excellence study titled Molecular Markers, Health Behaviors, and Comorbidities as Predictors of Tumor Recurrence, Survival, and Quality of Life in Head and Neck Cancer. This substudy was designed to determine the predictors of poor sleep among head and neck cancer patients 1 year after diagnosis. The dependent variable was a self-assessed sleep score 1 year after diagnosis. The independent variables were pain, xerostomia, treatment received (radiation, chemotherapy, and/or surgery), presence of a feeding tube and/or tracheotomy, tumor site and stage, comorbidities, depression, smoking, problem drinking, age, and sex.

SUBJECTS
Subjects were recruited from the University of Michigan Health System, the Henry Ford Health System, and the Veterans Affairs Ann Arbor Healthcare System otolaryngology clinics (Ann Arbor and Detroit, MI). Newly diagnosed patients with head and neck squamous cell carcinoma were eligible to participate. Excluded were those: 1) <18 years of age; 2) pregnant; 3) non-English speaking; 4) psychologically or mentally unstable (such as patients with suicidal ideation, acute psychosis, or dementia); or 5) with non-upper aerodigestive tract cancer (such as thyroid or cutaneous neoplasms). Of 1,054 patients initially approached for the larger study, 823 agreed to participate. Of those, 66 subjects were excluded leaving a sample of 757 in the larger study. For this substudy, an additional 84 did not complete the baseline health survey and 165 did not return a 1-year health survey. Additionally, another 51 subjects were excluded from these analyses due to missing data, resulting in a sample of 457. Retention of the sample was determined primarily by mortality. Of the 165 patients not retained, 110 (67%) had died.

PROCEDURES
Institutional review board approval was obtained at each site before the study. For the larger study, which began recruitment in 2003, research assistants approached patients in the waiting rooms of otolaryngology clinics for participation in the study. The research assistants obtained informed consent from all eligible patients who agreed to participate, who then were asked to complete a written survey on quality of life, health behaviors, and demographics. Clinical measures were collected by chart abstraction. Subjects were then resurveyed 1 year after diagnosis.

Measures
Dependent variable. Although sleep quality can be assessed objectively by a number of different modalities, including polysomnography, sleep latency testing, and actigraphy, self-reported questionnaires serve as a noninvasive substitute that have been validated and verified as useful instruments for research and clinical practice. The Medical Outcomes Study (MOS) sleep measure represents four constructs related to sleep health: sleep disturbance, adequacy of sleep, somnolence, and respiratory problems. It has been validated in two pilot studies, in a large sample of chronically ill patients, and in patients enrolled in ongoing clinical trials. The MOS sleep measure was administered initially and then again 1 year after diagnosis. The short-form index of six questions was used, which were averaged and transformed to a scale of 0 to 100, with 0 being the worst and 100 the best (mean score in a normal population was 72).

Independent variables. Pain was measured using the bodily pain score from the validated Short Form-36 (SF-36); low scores indicate worse pain. Xerostomia was measured by a question taken from the validated Head and Neck Quality of Life, a disease-specific quality-of-life instrument for patients with head and neck cancer that asked: As a result of your head and neck condition or treatment, over the past 4 weeks, how much have you been bothered by problems with dryness in your mouth while eating? The question was rated on a 5-point Likert scale as either not at all, slightly, moderately, a lot, or extremely.

Comorbidities were measured by chart abstraction using the Adult Comorbidity Evaluation-27 (ACE-27), a validated comorbidity index designed to evaluate levels of comorbidity for predicting survival and quality of life in head and neck cancer patients. The score on the ACE-27 was classified into two groups: moderate/severe comorbidity versus none/mild comorbidity. Other clinical measures abstracted from the patient medical records included tumor site, tumor stage, and treatment modality (including radiation, chemotherapy, and any head and neck surgery). Information on whether the patient had a feeding tube or tracheotomy at the time of the 1-year survey was also recorded. Tumor site was segregated into three groups for multivariate analysis: oral cavity/sinus; pharynx (oropharynx, hypopharynx, nasopharynx, or unknown primary); and larynx. Tumor stage was dichotomized into stage IV versus all others.

Depression was measured using the Geriatric Depression Scale-Short Form (GDS-SF); a score of 4 or higher on the GDS-SF indicates probable depression. Anyone smoking cigarettes within the last month was considered a smoker. The 10-item Alcohol Use Disorder Identification Test (AUDIT) was used to assess the level
of alcohol intake and related problems; a score of 8 or higher on the AUDIT indicates high risk of alcohol-related disorders. Because age and sex have been associated with sleep disturbances, they were also included in the analyses as predictor variables.

**Data Analysis**

Descriptive statistics were calculated for all measures; frequencies and percentages were presented for categorical variables, and means and standard deviations were presented for quantitative measures. Bivariate associations between the predictor variables and the outcome of 1-year sleep scores were calculated using Student t tests and analysis of variance. Student t tests were used to compare the sleep scores among patients with glottic cancer who were treated with organ-sparing therapy with the scores of patients treated with laryngectomy. Multiple linear regression was used to determine significant predictors of 1-year MOS sleep score.

**RESULTS**

**Quality of Sleep Characteristics**

The quality of sleep characteristics are shown in Table I. The mean sleep score at the time of diagnosis was 67.1. One year after diagnosis, the mean sleep score was slightly improved at 69.3 (P = .01). At 1 year, the mean SF-36 bodily pain score was 65.3. Forty-three percent of patients described their xerostomia as “a lot” or “extremely” bothersome at 1 year. Most had radiation, and over one half had chemotherapy and radiation. Most had cancer of the pharynx, over one half were stage IV, and over two thirds had none or mild comorbidities. About 36% had primary site surgery, 42% had a neck dissection, only 17% had a feeding tube, and <4% had a tracheotomy. One year after diagnosis, 19% of patients continued to smoke, 11% were problem drinkers, and 49% had positive depression screens. The mean age was 58 and over three quarters were male.

**Bivariate Analysis**

Bivariate analyses (Table II) showed that 1 year after diagnosis, increasing age in decades was statistically associated with higher sleep scores (P < .001). Female patients had significantly worse sleep at 1 year than male patients (P = .04). At 1 year, the bodily pain domain of the SF-36 was highly associated with the sleep score, with sleep scores 4.35 points higher for every 10 points improved bodily pain score (P < .001). The 1-year bodily pain score alone explained 30% of the variance in the 1-year sleep score. Xerostomia was highly correlated with 1-year sleep scores, with an average 25-point decrement in sleep scores between patients who had no complaints of dryness while eating versus those who were extremely bothered by dryness while eating (P < .001).

At 1 year after diagnosis, neither radiation, chemotherapy, nor any type of surgery (tumor extirpation from primary site or neck, laryngectomy, or reconstruction) affected sleep scores. Patients with glottic cancer who were treated with larynx-preserving therapy (n = 97) had no differences in sleep scores compared with patients treated with laryngectomy (n = 19) (P = .99). Patients who had a feeding tube at 1 year had a lower sleep score when compared to patients who did not (P = .005). Patients who had a tracheotomy at 1 year also had significantly lower sleep scores compared to those who did not (P = .001). Cancer site and stage were not associated with mean sleep score. At 1 year, moderate or severe comorbidities were only marginally associated with worse sleep scores (P = .068).

Depression and current smoking were both associated with large decrements in sleep score (P < .001). Patients with alcohol problems at 1 year had significantly worse sleep than those without an alcohol problem (P < .001).

**Multivariate Analysis**

Multivariate analyses (Table III) showed that SF-36 bodily pain score, xerostomia, presence of a tracheotomy, moderate/severe comorbidities, depressive symptoms at 1 year, and younger age were statistically significant predictors of worse sleep scores. A 1-point decrement in bodily pain score correlated with a nearly 2.2-point decrement in sleep score. A one-level decrement in the patient's score for xerostomia was associated with a 2.8-point decrease in sleep score.

Those with a current tracheotomy at 1 year averaged an 8.2-point decrement in sleep score. Although comorbidities were only marginally significant in the bivariate analyses, it became significant in the multivariate analyses; patients with moderate/severe comorbidities had a 4.0-point lower score when compared to patients with none/mild comorbidities. Depression was associated with a 14.3-point decrease in sleep score. Older patients had improved sleep scores (2.4 points for every decade in age).

Although presence of a feeding tube was significant on the bivariate analysis, it was no longer significant on the multivariate analysis. Moreover, smoking, alcohol problem, and sex were significant on the bivariate analyses, but were only marginally significant in the multivariate analyses. Radiation, chemotherapy, surgery, cancer site, and cancer stage were not significant in either the bivariate or multivariate analyses.

**DISCUSSION**

Sleep scores did not change dramatically from the time of diagnosis to 1 year after treatment. However, the scores at both time points are worse than the mean score for a normal population. It is likely that patients at baseline had poor sleep directly related to symptoms of their neoplasm, such as pain, coupled with anxiety related to their recent cancer diagnosis. Although one might expect that some or all of these factors would presumably improve after treatment, pain, xerostomia, and other discomforts related to treatment as well as fear of recurrence are likely to persist after treatment. This
may explain the relatively minor change in sleep scores from baseline to 1 year. Many variables contribute to the quality of sleep of head and neck cancer patients as outlined below.

**Pain**

Bodily pain was a strong predictor of worsened sleep scores. The relationship between pain and sleep in head and neck cancer patients has been previously demonstrated.\(^{23}\) Patients with chronic pain have identified sleep-related complaints as one of the most important aspects of their daily life on which pain has a deleterious effect.\(^{24}\) Pain is common among head and neck cancer patients, is commonly associated with insomnia, and clearly impacts health-related quality of life.\(^{25}\) This substantiates the need to aggressively treat pain in the head and neck cancer population.

**Xerostomia**

Xerostomia has been demonstrated to adversely affect quality of life in patients undergoing external beam radiation therapy, specifically with regard to fatigue and insomnia.\(^{11}\) Xerostomia most likely negatively impacts the sleep cycle because affected patients experience discomfort, and drink large quantities of liquids during the night, thereby fostering nocturnal micturition, frequent awakenings, and difficulty returning to sleep once awake. Hence, any potential alterations in treatment that might preserve salivary function could conceivably improve sleep quality. Intensity-modulated radiation therapy (IMRT) delivers increased doses of radiation to tumor or high-risk tissues, with relative sparing of functional tissue such as the salivary glands.\(^{26}\) The technique of sparing parotid glands in head and neck cancer external beam radiation protocols has been proven feasible and effective in preventing xerostomia.\(^{27}\) Xerostomia that disrupts sleep may also be related to submandibular gland dysfunction, as these glands produce the majority of basal salivary flow.\(^{28}\) The submandibular glands are not spared with IMRT; their role in xerostomia-related sleep disturbances has not been examined critically.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>457</td>
<td>58.3</td>
<td>10.6</td>
<td>23-92</td>
</tr>
<tr>
<td>Baseline sleep score</td>
<td>438</td>
<td>67.1</td>
<td>20.8</td>
<td>0-100</td>
</tr>
<tr>
<td>1-yr sleep score</td>
<td>457</td>
<td>69.3</td>
<td>20.6</td>
<td>0-100</td>
</tr>
<tr>
<td>Bodily pain, SF-36, 1 yr</td>
<td>457</td>
<td>65.3</td>
<td>26.0</td>
<td>0-100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerostomia, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>96</td>
<td>21.0</td>
</tr>
<tr>
<td>Slightly</td>
<td>78</td>
<td>17.1</td>
</tr>
<tr>
<td>Moderately</td>
<td>85</td>
<td>18.6</td>
</tr>
<tr>
<td>A lot</td>
<td>122</td>
<td>26.7</td>
</tr>
<tr>
<td>Extremely</td>
<td>76</td>
<td>16.6</td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>389</td>
<td>85.1</td>
</tr>
<tr>
<td>No</td>
<td>68</td>
<td>14.9</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>284</td>
<td>62.1</td>
</tr>
<tr>
<td>No</td>
<td>173</td>
<td>37.9</td>
</tr>
<tr>
<td>Surgery (any)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>240</td>
<td>52.5</td>
</tr>
<tr>
<td>No</td>
<td>217</td>
<td>47.5</td>
</tr>
<tr>
<td>Primary Site Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>162</td>
<td>35.5</td>
</tr>
<tr>
<td>No</td>
<td>295</td>
<td>64.5</td>
</tr>
<tr>
<td>Neck Dissection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>191</td>
<td>41.8</td>
</tr>
<tr>
<td>No</td>
<td>266</td>
<td>58.2</td>
</tr>
<tr>
<td>Feeding Tube, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>77</td>
<td>16.9</td>
</tr>
<tr>
<td>No</td>
<td>380</td>
<td>83.1</td>
</tr>
<tr>
<td>Tracheotomy, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17</td>
<td>3.7</td>
</tr>
<tr>
<td>No</td>
<td>440</td>
<td>96.3</td>
</tr>
<tr>
<td>Cancer Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharynx*</td>
<td>247</td>
<td>54.1</td>
</tr>
<tr>
<td>Oral cavity/sinus</td>
<td>94</td>
<td>20.6</td>
</tr>
<tr>
<td>Larynx</td>
<td>116</td>
<td>25.4</td>
</tr>
<tr>
<td>Cancer Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10</td>
<td>2.2</td>
</tr>
<tr>
<td>1</td>
<td>57</td>
<td>12.5</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>11.6</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>15.5</td>
</tr>
<tr>
<td>4</td>
<td>266</td>
<td>58.2</td>
</tr>
<tr>
<td>ACE-27 comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>130</td>
<td>28.5</td>
</tr>
<tr>
<td>Mild</td>
<td>191</td>
<td>41.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>96</td>
<td>21.0</td>
</tr>
<tr>
<td>Severe</td>
<td>40</td>
<td>8.7</td>
</tr>
<tr>
<td>Depressed, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>209</td>
<td>48.8</td>
</tr>
</tbody>
</table>

**TABLE I.**


<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>457</td>
<td>58.3</td>
<td>10.6</td>
<td>23-92</td>
</tr>
<tr>
<td>Baseline sleep score</td>
<td>438</td>
<td>67.1</td>
<td>20.8</td>
<td>0-100</td>
</tr>
<tr>
<td>1-yr sleep score</td>
<td>457</td>
<td>69.3</td>
<td>20.6</td>
<td>0-100</td>
</tr>
<tr>
<td>Bodily pain, SF-36, 1 yr</td>
<td>457</td>
<td>65.3</td>
<td>26.0</td>
<td>0-100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerostomia, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>96</td>
<td>21.0</td>
</tr>
<tr>
<td>Slightly</td>
<td>78</td>
<td>17.1</td>
</tr>
<tr>
<td>Moderately</td>
<td>85</td>
<td>18.6</td>
</tr>
<tr>
<td>A lot</td>
<td>122</td>
<td>26.7</td>
</tr>
<tr>
<td>Extremely</td>
<td>76</td>
<td>16.6</td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>389</td>
<td>85.1</td>
</tr>
<tr>
<td>No</td>
<td>68</td>
<td>14.9</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>284</td>
<td>62.1</td>
</tr>
<tr>
<td>No</td>
<td>173</td>
<td>37.9</td>
</tr>
<tr>
<td>Surgery (any)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>240</td>
<td>52.5</td>
</tr>
<tr>
<td>No</td>
<td>217</td>
<td>47.5</td>
</tr>
<tr>
<td>Primary Site Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>162</td>
<td>35.5</td>
</tr>
<tr>
<td>No</td>
<td>295</td>
<td>64.5</td>
</tr>
<tr>
<td>Neck Dissection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>191</td>
<td>41.8</td>
</tr>
<tr>
<td>No</td>
<td>266</td>
<td>58.2</td>
</tr>
<tr>
<td>Feeding Tube, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>77</td>
<td>16.9</td>
</tr>
<tr>
<td>No</td>
<td>380</td>
<td>83.1</td>
</tr>
<tr>
<td>Tracheotomy, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17</td>
<td>3.7</td>
</tr>
<tr>
<td>No</td>
<td>440</td>
<td>96.3</td>
</tr>
<tr>
<td>Cancer Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharynx*</td>
<td>247</td>
<td>54.1</td>
</tr>
<tr>
<td>Oral cavity/sinus</td>
<td>94</td>
<td>20.6</td>
</tr>
<tr>
<td>Larynx</td>
<td>116</td>
<td>25.4</td>
</tr>
<tr>
<td>Cancer Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10</td>
<td>2.2</td>
</tr>
<tr>
<td>1</td>
<td>57</td>
<td>12.5</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>11.6</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>15.5</td>
</tr>
<tr>
<td>4</td>
<td>266</td>
<td>58.2</td>
</tr>
<tr>
<td>ACE-27 comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>130</td>
<td>28.5</td>
</tr>
<tr>
<td>Mild</td>
<td>191</td>
<td>41.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>96</td>
<td>21.0</td>
</tr>
<tr>
<td>Severe</td>
<td>40</td>
<td>8.7</td>
</tr>
<tr>
<td>Depressed, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>209</td>
<td>48.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoked past month, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
<td>18.8</td>
</tr>
<tr>
<td>No</td>
<td>371</td>
<td>81.2</td>
</tr>
<tr>
<td>Alcohol problem, 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>49</td>
<td>10.7</td>
</tr>
<tr>
<td>No</td>
<td>409</td>
<td>89.3</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>353</td>
<td>77.2</td>
</tr>
<tr>
<td>Female</td>
<td>104</td>
<td>22.8</td>
</tr>
</tbody>
</table>

\(\text{SD} = \text{standard deviation}; \text{SF-36} = \text{Short Form-36}; \text{ACE-27} = \text{Adult Comorbidity Evaluation-27.}\)

*Pharynx cancer site includes Oropharynx, Hypopharynx, Nasopharynx, and Unknown Primary.

may explain the relatively minor change in sleep scores from baseline to 1 year. Many variables contribute to the quality of sleep of head and neck cancer patients as outlined below.

**Pain**

Bodily pain was a strong predictor of worsened sleep scores. The relationship between pain and sleep in head and neck cancer patients has been previously demonstrated.\(^{23}\) Patients with chronic pain have identified sleep-related complaints as one of the most important aspects of their daily life on which pain has a deleterious effect.\(^{24}\) Pain is common among head and neck cancer patients, is commonly associated with insomnia, and clearly impacts health-related quality of life.\(^{25}\) This substantiates the need to aggressively treat pain in the head and neck cancer population.

**Xerostomia**

Xerostomia has been demonstrated to adversely affect quality of life in patients undergoing external beam radiation therapy, specifically with regard to fatigue and insomnia.\(^{11}\) Xerostomia most likely negatively impacts the sleep cycle because affected patients experience discomfort, and drink large quantities of liquids during the night, thereby fostering nocturnal micturition, frequent awakenings, and difficulty returning to sleep once awake. Hence, any potential alterations in treatment that might preserve salivary function could conceivably improve sleep quality.

Intensity-modulated radiation therapy (IMRT) delivers increased doses of radiation to tumor or high-risk tissues, with relative sparing of functional tissue such as the salivary glands.\(^{26}\) The technique of sparing parotid glands in head and neck cancer external beam radiation protocols has been proven feasible and effective in preventing xerostomia.\(^{27}\) Xerostomia that disrupts sleep may also be related to submandibular gland dysfunction, as these glands produce the majority of basal salivary flow.\(^{28}\) The submandibular glands are not spared with IMRT; their role in xerostomia-related sleep disturbances has not been examined critically.
Future studies from our institution are planned to test whether salivary gland-sparing IMRT explains the better functional outcomes in patients subjected to radiation who do not complain of dry mouth. Based on our results, minimizing xerostomia appears worthwhile to improve postradiation sleep quality.

Treatments and Cancer Site and Stage

Although reports of the effect of radiation treatment and sleep have been mixed, we did not find an association between radiation and sleep quality.23,29 Nor did we find an association between chemotherapy, surgery, and presence of a feeding tube with sleep scores. Laryngectomized patients did not have any difference in sleep scores compared with those patients with glottic cancer who preserved their larynx; this directly contrasts with the findings of Boscolo-Rizzo et al.30 Moreover, cancer site and cancer stage did not predict sleep quality. Perhaps the numerous control variables in this study were able to tease out the fact that symptoms, such as pain and xerostomia, were more predictive of sleep quality than the actual treatments themselves. It may appear incongruous that patients receiving external beam radiation did not have lower sleep scores despite the strong association between xerostomia and worse sleep. We postulate that the size of our cohort, with its large percentage of patients who received some type of external beam radiation (either salivary-sparing or not) allowed for the statistical analysis to distinguish between those patients with xerostomia (approximately one half of those who received radiation) and those who did not complain of dry mouth despite also having received radiation. We expect that salivary gland-sparing techniques help prevent or limit the severity of xerostomia. As a result, xerostomia would be expected to be a stronger predictor of worse sleep scores than would external beam radiation itself. We therefore hypothesize that patients receiving parotid-sparing radiation therapy would have better sleep scores than patients receiving non-parotid sparing radiation therapy.

On the other hand, the presence of a tracheotomy tube 1 year after diagnosis was associated with a decrease in sleep score, and remained an independent predictor of 1-year sleep in the multivariate regression. Multiple studies suggest that head and neck cancer patients are predisposed to obstructive sleep apnea, although the data are far from conclusive.31 Theoretically, the presence of a tracheotomy would improve sleep in this patient group, which would not correlate with our

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>Mean Sleep Score</th>
<th>SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (decades)</td>
<td>3.8</td>
<td>0.9</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SF-36 pain (10 points), 1 yr</td>
<td>4.35</td>
<td>0.3</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Xerostomia, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>96</td>
<td>78.6</td>
<td>17.1</td>
<td></td>
</tr>
<tr>
<td>Slightly</td>
<td>78</td>
<td>70.7</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>Moderately</td>
<td>85</td>
<td>71.8</td>
<td>18.6</td>
<td></td>
</tr>
<tr>
<td>A lot</td>
<td>122</td>
<td>69.0</td>
<td>20.1</td>
<td></td>
</tr>
<tr>
<td>Extremely</td>
<td>76</td>
<td>53.5</td>
<td>21.4</td>
<td></td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>389</td>
<td>68.9</td>
<td>20.9</td>
<td>.378</td>
</tr>
<tr>
<td>No</td>
<td>68</td>
<td>71.3</td>
<td>19.1</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>284</td>
<td>68.3</td>
<td>21.0</td>
<td>.194</td>
</tr>
<tr>
<td>No</td>
<td>173</td>
<td>70.9</td>
<td>19.9</td>
<td></td>
</tr>
<tr>
<td>Surgery (any)</td>
<td></td>
<td></td>
<td></td>
<td>.974</td>
</tr>
<tr>
<td>Yes</td>
<td>240</td>
<td>69.3</td>
<td>20.6</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>217</td>
<td>69.2</td>
<td>20.7</td>
<td></td>
</tr>
<tr>
<td>Primary site surgery</td>
<td></td>
<td></td>
<td></td>
<td>.732</td>
</tr>
<tr>
<td>Yes</td>
<td>162</td>
<td>68.8</td>
<td>20.2</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>295</td>
<td>69.5</td>
<td>20.8</td>
<td></td>
</tr>
<tr>
<td>Neck dissection</td>
<td></td>
<td></td>
<td></td>
<td>.796</td>
</tr>
<tr>
<td>Yes</td>
<td>191</td>
<td>69.6</td>
<td>20.9</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>266</td>
<td>69.1</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>Feeding tube, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Yes</td>
<td>77</td>
<td>63.2</td>
<td>20.3</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>380</td>
<td>70.5</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>Tracheotomy, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Yes</td>
<td>17</td>
<td>53.3</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>440</td>
<td>69.9</td>
<td>20.2</td>
<td></td>
</tr>
<tr>
<td>Cancer site</td>
<td></td>
<td></td>
<td></td>
<td>.348</td>
</tr>
<tr>
<td>Pharynx*</td>
<td>247</td>
<td>70.3</td>
<td>20.7</td>
<td></td>
</tr>
<tr>
<td>Oral cavity/sinus</td>
<td>94</td>
<td>66.7</td>
<td>20.2</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>116</td>
<td>69.1</td>
<td>20.7</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td></td>
<td></td>
<td></td>
<td>.452</td>
</tr>
<tr>
<td>Yes</td>
<td>266</td>
<td>68.7</td>
<td>21.8</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>191</td>
<td>70.1</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td>.068</td>
</tr>
<tr>
<td>None/mild</td>
<td>321</td>
<td>70.4</td>
<td>20.3</td>
<td></td>
</tr>
<tr>
<td>Moderate/severe</td>
<td>136</td>
<td>66.6</td>
<td>21.0</td>
<td></td>
</tr>
<tr>
<td>Depressed, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Yes</td>
<td>176</td>
<td>54.7</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>281</td>
<td>78.4</td>
<td>16.3</td>
<td></td>
</tr>
<tr>
<td>Smoked past month, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
<td>57.6</td>
<td>20.7</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>371</td>
<td>72.0</td>
<td>19.6</td>
<td></td>
</tr>
<tr>
<td>Alcohol problem, 1 yr</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Yes</td>
<td>49</td>
<td>54.4</td>
<td>20.6</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>408</td>
<td>71.1</td>
<td>19.9</td>
<td></td>
</tr>
</tbody>
</table>

TABLE II. (Continued.)

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Mean Sleep Score</th>
<th>SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>353</td>
<td>70.3</td>
<td>20.8</td>
<td>.040</td>
</tr>
<tr>
<td>Female</td>
<td>104</td>
<td>65.6</td>
<td>19.6</td>
<td></td>
</tr>
</tbody>
</table>

Short Form-36 = SF-36; SD = standard deviation.†The SF-36 Bodily Pain Score and the MOS Sleep Score are measured on a scale of 0–100 with 100 being the best score.

*Pharynx cancer site includes Oropharynx, Hypopharynx, Nasopharynx, and Unknown Primary.

Shuman et al.: Sleep and Head and Neck Cancer
and poor quality of life has been conflicting. The establishment of the relationship between increased comorbidity and neck cancer has been proven, although data establishing between increased mortality and comorbidity in head and neck cancers is limited. 

Laryngoscope 120: June 2010 Shuman et al.: Sleep and Head and Neck Cancer

Depressive Symptoms

Consistent with the literature, depression is quite common in head and neck cancer patients and associated with poor sleep quality. Careful screening for depression in head and neck cancer patients complaining of sleep disturbances is needed, especially given the fact that effective counseling and medication therapies are available to treat clinical depression. Given the anticholinergic side effects of certain antidepressants and the high incidence of xerostomia in this patient population, clinicians ought to query patients with depression about xerostomia and carefully consider which medications may be better tolerated among depressed patients with head and neck cancer.

Smoking and Problem Drinking

Both smoking and drinking were significant predictors of 1-year sleep quality in the bivariate analyses, but were only marginally significant in the multivariate analyses. Although the research on sleep quality among smokers is limited, a large controlled trial demonstrated significantly altered sleep architecture detected during polysomnography in smokers, compared with nonsmokers and former smokers. Nicotine is a stimulant that can keep people awake. Moreover, nicotine cravings can arouse people from sleep. Because tobacco use is a major causative agent for head and neck cancer, and smoking predicts survival in this population, cessation services must be readily available to head and neck cancer patients; an added benefit may be improved sleep quality.

Patients with alcohol problems slept poorly compared with their counterparts, although the association was only marginally significant in the multivariate analysis. Alcohol’s direct negative effects on sleep are well-known. In addition, alcohol is synergistic with narcotics, on which many head and neck cancer patients rely. From a practical standpoint, these results confirm the need to monitor and screen for alcohol dependence not only at the time of diagnosis, but also during surveillance after treatment is complete.

Age and Sex

Younger patients with head and neck cancer had significantly worse sleep than their older counterparts in this study. This corroborates previous results, but is contrary to the generally observed trend of worsening sleep in older populations. Rogers et al. suggest that this may be due to a matter of perception (younger patients are more bothered by sleep disturbances, whereas older patients expect it). There may be a methodological limitation as well, as some data suggest that subjective and objective measurements of sleep in the elderly may be incongruous. Although studies have shown that women have lower sleep scores than men, sex was only marginally significant in the multivariate analysis. This suggests that other factors, such as symptoms and health behaviors, may override the effects of sex on sleep among head and neck cancer patients.

CONCLUSION

The independent variables of pain and xerostomia were major predictors of poor sleep quality among head and neck cancer patients. The presence of a tracheotomy,

<table>
<thead>
<tr>
<th>Variable Parameter Estimate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 bodily pain, 1 yr†</td>
<td>2.18</td>
</tr>
<tr>
<td>Xerostomia, 1 yr‡</td>
<td>−2.79</td>
</tr>
<tr>
<td>Radiation</td>
<td>−0.30</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1.19</td>
</tr>
<tr>
<td>Head and neck surgery (any)</td>
<td>1.06</td>
</tr>
<tr>
<td>Current feeding tube</td>
<td>0.83</td>
</tr>
<tr>
<td>Current tracheotomy</td>
<td>−8.22</td>
</tr>
<tr>
<td>Cancer site (vs. larynx)</td>
<td></td>
</tr>
<tr>
<td>Oral/sinus</td>
<td>−0.04</td>
</tr>
<tr>
<td>Pharynx*</td>
<td>−0.62</td>
</tr>
<tr>
<td>Stage IV cancer</td>
<td>0.74</td>
</tr>
<tr>
<td>Moderate/severe comorbidity</td>
<td>−3.97</td>
</tr>
<tr>
<td>Depressive symptoms, 1 yr</td>
<td>−14.27</td>
</tr>
<tr>
<td>Smoked past month, 1 yr</td>
<td>−3.43</td>
</tr>
<tr>
<td>Alcohol problem, 1 yr</td>
<td>−4.54</td>
</tr>
<tr>
<td>Age (decades)</td>
<td>2.39</td>
</tr>
<tr>
<td>Female gender</td>
<td>−3.08</td>
</tr>
</tbody>
</table>

†The SF-36 Bodily Pain Score and the MOS Sleep Score are measured on a scale of 0–100 with 100 being the best score.
‡Xerostomia is measured on a scale of 1–5 with 5 being the worst score.
*Pharynx cancer site includes Oropharynx, Hypopharynx, Nasopharynx, and Unknown Primary.
comorbidities, depression, and younger age were statistically significant predictors of poor sleep 1 year after diagnosis with head and neck cancer, whereas smoking and problem drinking were marginally significant. Cancer site and cancer stage did not predict sleep quality. Many factors adversely affecting sleep in head and neck cancer patients are potentially modifiable (particularly pain, xerostomia, depression, smoking, and problem drinking). All clinicians involved in the treatment of head and neck cancer patients can ably evaluate these entities, which is especially important given that the targeted treatment of these disorders is likely to improve sleep quality and quality of life.

BIBLIOGRAPHY