Obstructive Sleep Apnea After Radial Forearm Free Flap Reconstruction of the Oral Tongue

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Objectives/Hypothesis: To determine whether radial forearm free flap reconstruction of the tongue after partial glossectomy is associated with obstructive sleep apnea.

Study Design: Retrospective case series.

Methods: Fifteen patients (5 men, 10 women) treated for tongue cancer in 2006–2010 by partial glossectomy and immediate radial forearm free flap reconstruction completed the Epworth Sleepiness Scale and underwent polysomnographic studies. Background, clinical, and pathologic data were collected from the medical files.

Results: Mean ± SD age of the study group was 57 ± 19 years; body mass index, 24 ± 4; follow-up, 5.6 ± 2.8 years. Mean ± SD Epworth scale score was 8.18 ± 6.18 (normal, <8). Disordered sleep was documented in 11 patients, of whom 8 (53.3% of the cohort) had OSA (5 mild, 2 moderate, 1 severe). The OSA rate was significantly higher than reported in the general population (P = 0.001).

Conclusion: Patients after partial glossectomy and radial forearm free flap reconstruction appear to be at high risk of obstructive sleep apnea. Testing for OSA should be considered in these patients.

Key Words: Sleep apnea, tongue cancer, forearm free flap, quality of life.

Level of Evidence: Level IV.

INTRODUCTION

Episodes of apnea during sleep, defined as a cessation of airflow for 10 seconds or more, are caused by a relaxation of the upper airway dilator muscles and the concomitant loss of a patent upper airway. They may lead to ventilatory effort against the partially or completely obstructed airway. Repetitive obstructive sleep apnea (OSA) episodes are associated with recurrent oxyhemoglobin desaturation and arousals from sleep. OSA has been linked to various cardiovascular morbidities, including metabolic syndrome, systemic hypertension, myocardial infarction, and cerebrovascular complications, and an increased mortality risk.\(^1\)\(^2\) The reported incidence of OSA in the general population is 4% in middle-aged men and 2% in middle-aged women. Male sex and obesity are strongly associated with the disorder.\(^3\)

Few studies have addressed the issue of OSA and head and neck cancer treatment, with controversial findings. Friedman et al.\(^4\) documented OSA in 91% of patients following treatment for various head and neck tumors, whereas Nesse et al.\(^5\) reported a prevalence of only 12%. The cause of OSA secondary to head and neck cancer treatment is unclear as well. There are some anecdotal cases of OSA in patients treated by neck irradiation.\(^6\)\(^7\)

The treatment of tongue cancer usually consists of partial glossectomy and reconstruction with a soft tissue flap, such as a radial forearm free flap (RFFF). Patients generally regain a satisfactory quality of life in terms of speaking, eating, and social involvement.\(^8\) However, we speculate that because glossectomy and flap insertion alter the morphology, tone, and sensitivity of the tongue and oral cavity, sleep problems may occur. Moreover, many of these patients receive supplemental oncologic therapy, which can aggravate sleep-disordered breathing.

The aim of this study was to evaluate the quality of sleep and the rate of sleep-disordered breathing in patients treated for tongue cancer with RFFF reconstruction.

MATERIALS AND METHODS

A retrospective clinical study design was used. The study sample consisted of patients with cancer of the mobile tongue attending a tertiary, university-affiliated medical center between 2006 and 2010. Patients were identified through the hospital’s cancer registry and cross-referenced with a head and neck surgical oncology registry. The present study included only those with newly diagnosed, previously untreated, and pathologically confirmed disease who underwent partial resection of the mobile tongue only, with no involvement of other subsites of the oral cavity, followed by reconstruction with a RFFF.

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Patients with distant metastases at presentation, a past history of head and neck malignancy, or disease recurrence during the study period were excluded, as were patients who refused treatment. Patients with previously known sleep-disordered breathing were excluded as well.

Of the 42 patients who presented with cancer of the mobile tongue during the study period, three had a prior history of OSA. Overall, 15 patients met the inclusion criteria. Their medical files were reviewed for sex, age, smoking habits, body mass index, medical history, tumor type and stage, and supplemental oncologic therapy. To evaluate the rate and severity of sleep apnea, the patients were asked during a routine follow-up visit to complete the Epworth Sleepiness Scale9 (Table I). In addition, polysonomography was performed in the sleep laboratory using the Compumedics e-Series, Profusion PSG device (version 1.01; Compumedics Ltd., Abbotsford, Victoria); sleep measurements were based on the criteria of the American Academy of Sleep Medicine.10 The apnea-hypopnea index (AHI), an index used to assess the severity of sleep apnea, based on the total number of apnea and hypopnea per hour of sleep, was retrieved from each sleep study. An AHI of >5 to ≤15 was defined as mild OSA, AHI of >15 to ≤30 as moderate OSA, and AHI of >30 as severe OSA. The study was approved by the Research Ethics Board of Rabin Medical Center, and all patients signed an informed consent form.

**Statistical Analysis**

Continuous variables are presented as arithmetic means and standard deviations (SD), and categorical variables as percentages. Age was analyzed both as a continuous and dichotomous variable (<60 years and ≥60 years). Binomial test was used to compare the rate of OSA between the study population and the general population, overall and by sex. Because the AHI was not normally distributed, we used the nonparametric Mann-Whitney test to compare values by patient sex and age. Spearman’s correlation was calculated between age, height, weight, body mass index (BMI), Epworth Sleepiness Scale score, tumor T stage, and AHI. Fisher’s exact test was used to evaluate the association of sex and age with AHI. Mann-Whitney test was used to compare patients with and without OSA for age, height, weight, BMI, Epworth Sleepiness Scale score, and tumor T stage. Two-sided \( P < 0.05 \) was considered statistically significant. Statistical analysis was performed using the IBM SPSS, version 19.

### RESULTS

The study group consisted of 10 women and 5 men of mean (±SD) age 57 ± 19 years (range 27–79 years) at presentation. Their clinical characteristics are shown in Table II. Mean height measured 163 ± 5.8 cm; weight 66.3 ± 13.1 kg; body mass index 24.1 ± 4.3. Five patients presented with early-stage (stage II) tumors and 10 patients presented with advanced-stage (III and IV) tumors. Four patients (26%) had clinical and/or radiographic evidence of nodal metastases at presentation (Table II). All underwent resection of one-third to one-half of the mobile tongue and selective neck dissection. Patients with N0 disease were treated with elective supraomohyoid (level 1–3) neck dissection, and patients with N1 disease were treated with level 1–4 dissection, as necessary. The tongue was reconstructed with a fasciocutaneous free flap taken from the radial forearm, measuring from between 5*5 cm to 7*6 cm (Table II). The final pathologic diagnosis was squamous cell carcinoma in 12 patients, and adenocarcinoma, mucoepidermoid carcinoma, and adenocystic carcinoma in one patient each. Thirteen patients received adjuvant radiotherapy; two of them also received chemotherapy. The average time from completion of treatment (including postoperative oncologic therapy) to OSA evaluation was 4.9 years (range 2–6 years). The mean duration of postoperative follow-up was 5.6 ± 2.8 years.

The mean score on the Epworth Sleepiness Scale was 8.18 ± 6.18 (normal, <8). Fifty percent of the

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**TABLE I.**

The Epworth Sleepiness Scale.

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>CHANCE OF DOZING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td></td>
</tr>
<tr>
<td>Watching TV</td>
<td></td>
</tr>
<tr>
<td>Sitting inactive in a public place (e.g., a theater or a meeting)</td>
<td></td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td></td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td></td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td></td>
</tr>
<tr>
<td>Sitting quietly after a lunch without alcohol</td>
<td></td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td></td>
</tr>
</tbody>
</table>

To check your sleepiness score, total the points. Check your total score to see how sleepy you are (http://www.stanford.edu/~dement/key.html). Accessed from: http://www.stanford.edu/~dement/epworth.html on 10/8/2012.
patients had a score lower than 8. Mean AHI was 8 ± 0.593, P = 0.042. There were no significant associations of AHI with sex, height, weight, BMI, or tumor T stage. There were no significant differences in age, height, weight, BMI, or tumor T stage between patients with or without OSA. The rate of OSA in the study population was significantly higher than reported in the general population (P = 0.001). Among the other three patients with disordered sleep, two had multiple arousals due to periodic leg movements, and one had a long sleep latency period (38–71 minutes).

DISCUSSION
Monitoring the sleep of patients after partial glossectomy and RFFF reconstruction yielded a 73% rate of disordered sleep and a 53% rate of OSA. The incidence of OSA found here is significantly higher than in the general population. Furthermore, in the general population OSA usually affects obese middle-aged people and twice as many men as women, with an equal distribution only between postmenopausal women and men. However, in the present study, the relative number of men and women with OSA was nearly equal (with more women than men), and none of the affected patients was obese. Body mass index varied from normal range to mild overweight.

Several factors may contribute to the increased incidence of OSA in patients treated for tongue cancer. Pathophysiologically, OSA occurs when the patency of the upper airway is not maintained during sleep. This may be due to the presence of enlarged soft tissue in the oral cavity or oropharynx or narrowing of the pharyngeal space. Radial forearm flaps used for reconstruction of the tongue add an adynamic bulk to the oral cavity, and the sensorium of the reconstructed area is seldom regained. Alternatively, OSA may be caused by partial loss of the normal dilator and retractor musculature, such as the palatoglossus and geniohyoid, which is responsible for preventing the tongue from collapsing backward during sleep. Supplemental oncologic therapy may also exacerbate disordered breathing during sleep. Studies have shown that chemoradiation to the head and neck area can cause soft tissue changes with decreased elasticity and chronic edema; the edema may be exacerbated by hypothyroidism following radiation therapy. Chemotherapy or radiotherapy to the upper aerodigestive tract can increase fibrosis and impair elasticity, with scarring and narrowing of the airway. Damage to the salivary glands can lead to a lack of saliva, reducing lubrication of the oral and oropharyngeal mucosa, thereby increasing upper airway resistance.

A study by Qian et al. demonstrated that 73% of patients after RFFF reconstruction had OSA, with a respiratory disturbance index (RDI) of >15. Their study group included patients with oral and oropharyngeal carcinoma, and more than half had had a composite resection and reconstruction of the oral cavity and

<table>
<thead>
<tr>
<th>Pt. no.</th>
<th>Age (yr)/sex</th>
<th>Cancer Stage</th>
<th>Adjuvant Oncologic Therapy</th>
<th>Time from Treatment (yr)*</th>
<th>AHI</th>
<th>Degree of OSA</th>
<th>% Tongue Resected</th>
<th>Flap Size (cm*cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>79/M</td>
<td>T3n0</td>
<td>CR</td>
<td>4</td>
<td>12</td>
<td>Moderate</td>
<td>40%</td>
<td>7*5</td>
</tr>
<tr>
<td>2</td>
<td>27/F</td>
<td>T2N1</td>
<td>R</td>
<td>6</td>
<td>3</td>
<td>–</td>
<td>35%</td>
<td>5*5</td>
</tr>
<tr>
<td>3</td>
<td>63/M</td>
<td>T3N0</td>
<td>R</td>
<td>5</td>
<td>2</td>
<td>–</td>
<td>40%</td>
<td>6*6</td>
</tr>
<tr>
<td>4</td>
<td>44/F</td>
<td>T3N0</td>
<td>R</td>
<td>3</td>
<td>5</td>
<td>Mild</td>
<td>40%</td>
<td>6*6</td>
</tr>
<tr>
<td>5</td>
<td>78/M</td>
<td>T3N0</td>
<td>R</td>
<td>4</td>
<td>42</td>
<td>Severe</td>
<td>50%</td>
<td>7*6</td>
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<tr>
<td>6</td>
<td>29/F</td>
<td>T3N0</td>
<td>R</td>
<td>2</td>
<td>0</td>
<td>–</td>
<td>50%</td>
<td>6*6</td>
</tr>
<tr>
<td>7</td>
<td>70/M</td>
<td>T2N0</td>
<td>R</td>
<td>6</td>
<td>18</td>
<td>Moderate</td>
<td>40%</td>
<td>6*7</td>
</tr>
<tr>
<td>8</td>
<td>51/F</td>
<td>T2N1</td>
<td>CR</td>
<td>5</td>
<td>5</td>
<td>Mild</td>
<td>35%</td>
<td>6*6</td>
</tr>
<tr>
<td>9</td>
<td>43/F</td>
<td>T2N1</td>
<td>R</td>
<td>6</td>
<td>5</td>
<td>Mild</td>
<td>40%</td>
<td>6*6</td>
</tr>
<tr>
<td>10</td>
<td>78/F</td>
<td>T2N1</td>
<td>R</td>
<td>6</td>
<td>3</td>
<td>–</td>
<td>40%</td>
<td>6*6</td>
</tr>
<tr>
<td>11</td>
<td>71/F</td>
<td>T3N0</td>
<td>R</td>
<td>5</td>
<td>2</td>
<td>–</td>
<td>50%</td>
<td>7*6</td>
</tr>
<tr>
<td>12</td>
<td>46/M</td>
<td>T3N0</td>
<td>R</td>
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<td>7</td>
<td>–</td>
<td>50%</td>
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</tr>
<tr>
<td>13</td>
<td>78/F</td>
<td>T2N0</td>
<td>–</td>
<td>6</td>
<td>9</td>
<td>Moderate</td>
<td>35%</td>
<td>6*6</td>
</tr>
<tr>
<td>14</td>
<td>30/F</td>
<td>T2N0</td>
<td>–</td>
<td>4</td>
<td>0.7</td>
<td>–</td>
<td>35%</td>
<td>6*6</td>
</tr>
<tr>
<td>15</td>
<td>69/F</td>
<td>T2N0</td>
<td>R</td>
<td>5</td>
<td>8</td>
<td>Mild</td>
<td>40%</td>
<td>6*6</td>
</tr>
</tbody>
</table>

*Time from completion of treatment in years to PSG and ESS testing.
AHI = apnea/hypopnea index, CR = chemo-radiation, OSA = obstructive sleep apnea, R = radiation, RFFF = radial forearm free flap.
oropharynx. They suggested that surgical patients have a higher prevalence of moderate to severe OSA than nonsurgical patients. Their results imply that the RFFF reconstruction rather than the chemoradiation treatment is the main cause of the upper airway obstruction. Our study focused on patients after partial resection of the free tongue and RFFF reconstruction, showing that the rate of OSA was still very high.

Patients with cancer are often subject to fatigue from such causes as poor nutritional intake, anxiety, or depression. However, general complaints of tiredness and weariness tend to be overlooked.\textsuperscript{15} The Epworth Sleepiness Scale (Table I) measures OSA-related symptoms; a score of $>8$ is considered pathological.\textsuperscript{16} Qian et al.\textsuperscript{13} demonstrated a low reliability of the Epworth Sleepiness Scale in patients after surgery or chemoradiation for oral cavity cancer. In the present study, the mean score was $8.18 \pm 6.18$, and $50\%$ of the patients had a score lower than 8. The weak association of the sleep symptoms with the findings on sleep study may be attributable to the patients’ disregard of their general complaints and daytime fatigue. Thus, when discussing quality of life issues with patients after surgery for tongue cancer, clinicians must take sleep quality into account. As patient self-reports of symptoms may not be very reliable, polysomnographic evaluation should be considered in every case.

Patients after reconstructive surgery of the oral cavity are not likely to benefit from the classic surgical techniques for OSA, such as uvulopalatoplasty and tongue base surgery. However, they should all be offered treatment with continuous positive airway pressure (CPAP).\textsuperscript{13} In cases of severe OSA in patients who are noncompliant with CPAP, tracheotomy should be considered.

Sleep disorders are highly comorbid with other medical conditions. Periodic limb movement, also known as restless legs syndrome, is a neurologic disorder and a medical condition. Periodic limb movements require medical treatment for the neurologic disease (dopamine agonists may be useful)\textsuperscript{17} and referral to a psychiatrist for treatment of accompanying depression and anxiety.

**CONCLUSION**

Patients after partial glossectomy and RFFF reconstructive surgery appear to be at high risk of OSA compared to the general population. Testing for OSA and other sleep-related disorders should be studied further, but needs to be considered based on our findings in the group of patients reported here by us and by others reported in the literature.

**BIBLIOGRAPHY**