Impact of Head and Neck Radiotherapy for Patients With Nasopharyngeal Carcinoma on Sleep-Related Breathing Disorders

Hsin-Ching Lin, MD; Michael Friedman, MD; Hsueh-Wen Chang, PhD; Fu-Min Fang, MD, PhD; Meng-Chih Lin, MD; Mao-Chang Su, MD

IMPORTANCE Little is known about the relationships between sleep-related breathing disorders (SRBDs) and nasopharyngeal carcinoma (NPC).

OBJECTIVE To clarify the impact of head and neck radiotherapy on SRBDs, we performed a pilot study to investigate the change of sleep architecture in patients with NPC before and after treatment.

DESIGN, SETTING, AND PARTICIPANTS A retrospective review of a prospective data set of 18 patients with NPC (15 men and 3 women; mean age, 49.8 years) and symptoms of SRBD, who completed radiotherapy and underwent polysomnography before and after treatment at a university-affiliated tertiary referral center.

INTERVENTIONS Radiotherapy and/or chemotherapy were applied based on the NPC stage.

MAIN OUTCOMES AND MEASURES Subjective SRBD symptoms, Epworth sleepiness scale score, snoring severity (visual analog scale, rated 0-10 by bed partner), and objective full-night polysomnographic parameters (apnea-hypopnea index [AHI], AHI in rapid eye movement [REM] sleep, central sleep apnea index, percentage of light sleep, percentage of deep sleep, percentage of REM sleep, sleep efficiency, sleep latency, arousal index, mean oxygen saturation, lowest oxygen saturation, desaturation index, and snoring index) were collected before and at least 6 months after treatment.

RESULTS After treatment, Epworth sleepiness scale and snoring severity scores significantly decreased from a mean (SD) of 11.0 (5.0) to 7.8 (2.3) ($P = .005$) and 6.0 (3.4) to 2.8 (2.3) ($P < .001$), respectively. The AHI changed from 26.2 (28.4) to 21.67 (24.15) ($P = .28$). However, AHI increased in 8 of 18 patients. A statistically significant increase was shown in mean oxygen saturation, from 95.3% (2.0%) to 97.1% (1.4%) ($P < .001$), though lowest oxygen saturation was not significantly altered. Percentage of light sleep increased significantly from 78.9% (8.8%) to 86.1% (9.6%) ($P = .02$), and percentage of REM sleep decreased from 17.5% (6.4%) to 12.7% (8.9%) ($P = .10$). Percentage of deep sleep was not significantly altered.

CONCLUSIONS AND RELEVANCE Although the severity of apnea and hypopnea events and snoring decreased in most of the patients with NPC after treatment, the sleep architecture became disrupted and 8 of 18 of the patients had an increased AHI after treatment. Identification and treatment of obstructive sleep apnea and hypopnea in patients with NPC may be important factors for improving the quality of life.

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Author Affiliations: Author affiliations are listed at the end of this article.
Corresponding Author: Hsin-Ching Lin, MD, Department of Otolaryngology, Sleep Center, Kaohsiung Chang Gung Memorial Hospital, 123, Ta-Pei Rd, Niao-Sung District, Kaohsiung City, 833, Taiwan (enthclin@aol.com).
With increasing numbers of head and neck cancer (HNC) survivors over the past decades, focus within this population has shifted from survival to quality of life.1 A relatively high prevalence of sleep-related breathing disorders (SRBDs) within a population of patients with HNC has been reported2; however, little is known about the effects of HNC therapy on sleep disorders and vice versa. The implication is that recognition and treatment of obstructive sleep apnea-hypopnea syndrome (OSAHS) may play an important role in improving quality of life for these patients.

Nasopharyngeal carcinoma (NPC) is derived from the nasopharyngeal epithelium, primarily from the fossa of Rosenmüller. Radiotherapy and chemotherapy are the main stays of therapy for NPC because these tumors are biologically highly radiosensitive and chemosensitive. Furthermore, these tumors tend to metastasize early to the neck regions. Despite their awkward anatomical location, recurrent tumors are often resected with surgery and have achieved good oncological control. Hence, surgery is not the initial therapy because of the biological behavior of this cancer and is not dependent on accessibility, since modern skull base surgery has overcome many impasses regarding, for example, injury of internal carotid artery injury, cerebrospinal fluid leakage, and postoperative meningitis. Intuitively, it would be reasonable to assume that radiation therapy to the nasopharynx and neck could cause changes in the stability of the airway and the function of the upper airway dilator musculature, which in turn affects upper airway compliance and resistance. Thus, patients with NPC may be suitable candidates to evaluate the impact of radiotherapy on SRBD. To our knowledge, no study to date has specifically addressed the impact of radiotherapy of the head and neck region on objective and subjective indexes of sleep disturbance in this group of patients.

This study was initiated as a preliminary pilot to assess changes in respiratory sleep indexes, sleep architecture, and daytime somnolence before and after treatment in patients with NPC.

Methods

Approval for this retrospective study of a prospective group of patients was obtained from the institutional review board and ethics committee at Chang Gung Memorial Hospital. Medical records of all patients with NPC who completed radiotherapy plus or minus chemotherapy and underwent polysomnography (PSG) before and at a minimum of 6 months after treatment were reviewed. The recruited patients had no history of any upper airway surgery, chronic obstructive pulmonary disease, or any other head and neck malignancy. Only patients who completed NPC treatment and had complete pretreatment and posttreatment sleep study data and daytime sleepiness questionnaire with Epworth sleepiness scale (ESS) scores3 were included.

Radiotherapy

All patients were treated with either curative 3-dimensional conformal radiotherapy or intensity-modulated radiotherapy. The treatment delivered was determined by the preference of the treating physician and available departmental resources.

Chemotherapy

The patients were treated with a combination of systemic chemotherapy as adjuvant or concurrent sequence during the radiotherapy course. The regimens used involved a combination of cisplatin and fluorouracil administered intravenously and were determined at the discretion of the treating physician.

Sleep Study

Full-night, attended, comprehensive diagnostic sleep studies were performed at the sleep center of the Chang Gung Memorial Hospital–Kaohsiung Medical Center in a temperature-controlled and sound-attenuated room. Electroencephalography, submental electromyography, and electro-oculography data were recorded with surface electrodes by standard techniques. Nasal and oral airflow were recorded by thermistors. Oxygen saturation was measured by pulse oximetry. Sleep stage scoring was performed by experienced technicians according to the standard criteria.4 The severity of SRBD was classified according to the number of apneas and hypopneas observed during sleep. Obstructive apnea was defined as cessation of airflow for at least 10 seconds with corresponding respiratory effort. Obstructive hypopnea was defined as an abnormal respiratory event with at least 30% reduction in thoracoabdominal movement or airflow when compared with the baseline, lasting at least 10 seconds, and with 4% or greater oxygen desaturation.5 Apnea-hypopnea index (AHI) was defined as the total number of apneas and hypopneas per hour of electroencephalographic sleep. Central respiratory events were excluded for OSAHS severity classification. Obstructive sleep apnea-hypopnea syndrome was defined as an AHI of greater than 5 events per hour.6 All studies were scored and read by a sleep physician approved by the Board of Sleep Medicine in Taiwan. All pretreatment PSGs were performed within 2 weeks after confirming the diagnosis of NPC by endoscopic nasopharyngeal biopsy. It was usually from 2 weeks to 1 month before the patients began the NPC treatment.

Outcomes

Subjective SRBD symptoms, ESS score, and snoring visual analog scale (VAS; rated 0-10 by bed partner), as well as polysomnographic parameters, were collected before treatment and at a minimum of 6 months after completion of NPC treatment. Because currently no satisfactory objective test is indicative of the severity of daytime sleepiness in patients with SRBD, most physicians clinically use ESS to subjectively record the daytime fatigue status. In our study, we measured the patients’ daytime sleepiness with ESS score before and after treatment to respond to the changes of the degree of fatigue-related daytime sleepiness.

Polysomnographic outcomes of interest included AHI, AHI in rapid-eye-movement (REM) sleep, central sleep apnea (CSA) index, percentage of light sleep (stages 1 and 2 [S1 + S2]), percentage of deep sleep (stages 3 and 4 [S3 + S4]), percentage of REM sleep, sleep efficiency, sleep latency, arousal index, mean
Table I. Comparison of Subjective Estimates of Symptoms and Polysomnographic Data in 18 Patients* With Nasopharyngeal Carcinoma Before and 6 Months After Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baselineb</th>
<th>Posttreatmentb</th>
<th>Mean Difference (95% CI)</th>
<th>Change, Mean %</th>
<th>P Valuec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snoring VAS score (scale, 0-10)</td>
<td>6.0 (3.4)</td>
<td>2.8 (2.3)</td>
<td>−3.2 (−4.6 to −1.9)</td>
<td>−51.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ESS score</td>
<td>11.0 (5.0)</td>
<td>7.8 (2.3)</td>
<td>−3.2 (−5.6 to −0.8)</td>
<td>−14.2</td>
<td>.005</td>
</tr>
<tr>
<td>BMI</td>
<td>24.7 (4.27)</td>
<td>21.8 (3.0)</td>
<td>−2.8 (−4.1 to −1.6)</td>
<td>−10.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patients with OSAHS, No. (%)</td>
<td>13 (72)</td>
<td>14 (78)</td>
<td>NA</td>
<td>NA</td>
<td>.56</td>
</tr>
<tr>
<td>Mild, No.</td>
<td>3</td>
<td>6</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Moderate, No.</td>
<td>4</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Severe, No.</td>
<td>6</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>76.8 (15.3)</td>
<td>64.9 (24.9)</td>
<td>−11.9 (−24.1 to 0.3)</td>
<td>−14.1</td>
<td>.17</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>20.6 (19.5)</td>
<td>19.0 (17.7)</td>
<td>−1.6 (−9.8 to 6.7)</td>
<td>30.6</td>
<td>.47</td>
</tr>
<tr>
<td>Arousal index (per h)</td>
<td>31.7 (38.6)</td>
<td>25.6 (24.0)</td>
<td>−6.1 (−23.2 to 10.9)</td>
<td>16.7</td>
<td>.68</td>
</tr>
<tr>
<td>S1+S2, %</td>
<td>78.9 (8.8)</td>
<td>86.1 (9.6)</td>
<td>7.1 (0.8 to 13.5)</td>
<td>10.3</td>
<td>.02</td>
</tr>
<tr>
<td>S3+S4, %</td>
<td>3.3 (5.1)</td>
<td>1.2 (2.9)</td>
<td>−2.2 (−5.0 to 7.4)</td>
<td>127.2</td>
<td>.33</td>
</tr>
<tr>
<td>REM sleep, %</td>
<td>17.5 (6.4)</td>
<td>12.7 (8.9)</td>
<td>−4.8 (−10.4 to 0.8)</td>
<td>−8.9</td>
<td>.10</td>
</tr>
<tr>
<td>AHI (per h)</td>
<td>26.2 (28.4)</td>
<td>21.7 (24.2)</td>
<td>−4.6 (−12.2 to 3.1)</td>
<td>179.3</td>
<td>.28</td>
</tr>
<tr>
<td>Patients with worse AHI after NPC treatment, No. (%)</td>
<td>NA</td>
<td>8 (44)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>AHI in REM sleep (per h)</td>
<td>30.0 (26.9)</td>
<td>27.0 (20.2)</td>
<td>−2.9 (−15.8 to 9.9)</td>
<td>125.2</td>
<td>.77</td>
</tr>
<tr>
<td>CSA index</td>
<td>1.6 (3.1)</td>
<td>0.7 (1.3)</td>
<td>−0.9 (−2.7 to 0.9)</td>
<td>−7.3</td>
<td>.59</td>
</tr>
<tr>
<td>Longest apnea, s</td>
<td>36.2 (23.4)</td>
<td>48.0 (33.6)</td>
<td>11.8 (−2.4 to 25.9)</td>
<td>36.3</td>
<td>.10</td>
</tr>
<tr>
<td>Longest hypopnea, s</td>
<td>55.3 (24.4)</td>
<td>50.5 (29.0)</td>
<td>−4.8 (−18.6 to 9.0)</td>
<td>−9.7</td>
<td>.45</td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>95.3 (2.0)</td>
<td>97.1 (1.4)</td>
<td>1.9 (1.1 to 2.6)</td>
<td>2.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LSAT, %</td>
<td>83.1 (12.1)</td>
<td>85.3 (10.1)</td>
<td>2.3 (−3.9 to 8.4)</td>
<td>4.9</td>
<td>.66</td>
</tr>
<tr>
<td>Desaturation index (per h)</td>
<td>20.6 (24.7)</td>
<td>8.8 (17.6)</td>
<td>−11.8 (−19.6 to −40.0)</td>
<td>−26.1</td>
<td>.008</td>
</tr>
<tr>
<td>Snoring index (per h)</td>
<td>183.6 (169.7)</td>
<td>52.2 (68.8)</td>
<td>−131.4 (−226.7 to −36.0)</td>
<td>−96.3</td>
<td>.006</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CSA, central sleep apnea; ESS, Epworth sleepiness scale; LSAT, lowest oxygen saturation; NA, not applicable; NPC, nasopharyngeal carcinoma; OSAHS, obstructive sleep apnea-hypopnea syndrome; REM, rapid eye movement; S1 + S2, stages 1 and 2 (percentage of light sleep); S3 + S4, stages 3 and 4 (percentage of deep sleep); VAS, visual analog scale.

* Three female and 15 male (mean [SD] age, 49.8 [10.7] years).

b Data are given as mean (SD) value unless otherwise specified.

c By Wilcoxon signed rank test for paired data or Fisher exact test.

Results

A total of 18 patients with NPC met the criteria (15 men and 2 women; mean [SD] age, 49.8 [10.7] years; and mean [SD] body mass index [calculated as weight in kilograms divided by height in meters squared], 25.8 [4.3]). Baseline characteristics and pretreatment and posttreatment subjective and objective data are presented in Table 1. Each individual patient’s pretreatment and posttreatment AHI and LSAT are given in Table 2.

Six months after the treatment, the mean ESS and snoring VAS (0-10) scores were both significantly reduced following treatment, from 11.0 (5.0) to 7.8 (2.3) (P = .005) and 6.0 (3.4) to 2.8 (2.3) (P < .001), respectively.

The proportion of patients with mild OSAHS (AHI ≥5 to <15) increased from 16.7% to 33.3%, and the proportion of patients with moderate (AHI ≥15 to <30) or severe (AHI ≥30) OSAHS decreased from 56% to 44% following treatment, though these overall proportional changes of AHI were not statistically significant (P = .56). Although AHI improved in 10 patients (56%) of the 18 patients with NPC after treatment, AHI worsened in 8 (44%). Overall, the AHI reduction in these treated patients did not reach statistical significance, from the 26.2 (28.4) at pretreatment to 21.7 (24.2) after treatment (P = .28).

A statistically significant increase was shown in mO₂ from 95.3% (2.0%) to 97.1% (1.4%) (P < .001), though mean LSAT was not significantly altered (P = .66). Percentage of light sleep (S1+S2) increased significantly from 78.9% (8.8%) to 86.1% (9.6%) (P = .02) and percentage of REM sleep decreased from 17.5% (6.4%) to 12.7% (8.9%) (P = .10). Percentage of deep sleep (S3+S4) was not significantly altered (P = .33).

The incidence of OSAHS in these patients with NPC was 72% (13 of 18) before treatment and 78% (14 of 18) 6 months after treatment and posttreatment subjective and objective data are given in Table 1. Each individual patient’s pretreatment and posttreatment AHI and LSAT are given in Table 2.

Statistical Analysis

All collected data were tabulated in Microsoft Excel for Windows software version 2010 (Microsoft Corp). Continuous data are expressed as mean (SD) values. All analyses were conducted using the statistical software SAS version 9.2 (SAS Institute Inc). Pretreatment and posttreatment data were compared using the Wilcoxon signed rank test for paired data or the Fisher exact test, when appropriate. P < .05 was considered statistically significant.
after treatment. All patients who had an abnormal polysomnogram with an AHI higher than 15 or an AHI higher than 5 and combined obvious daytime hypersomnolence after treatment were referred for continuous positive airway pressure (CPAP) titration studies, and home therapy with CPAP was recommended. However, no patients continue to use CPAP on a regular basis because of severe dry mouth and worsening of the habitual sleep pattern.

**Discussion**

The pathophysiology of OSAHS is based on an inability to maintain upper airway patency during sleep. The cause of this inability varies considerably among patients but includes 3 categories of problems: (1) hypertrophy of soft tissues in the upper airway such as the adenoid, tonsils, soft palate, and tongue base; (2) narrowing of the upper airway space by facial skeletal anatomic abnormalities; or (3) impairment of both function and control of the pharyngeal dilator musculature. It is reasonable to suppose that patients with HNC, including those having undergone treatment with chemoradiation, might be affected by 1 or more of these abnormalities.

Several previous studies have examined the relationship between HNC, or the treatment of HNC and OSAHS. In a 2005 review, Rada7 noted that numerous authors had described the phenomenon of HNC first presenting as OSAHS, but there were relatively few studies assessing the incidence of OSAHS among patients with known HNC. To date, the majority of related studies have assessed either the pretreatment incidence of OSAHS among patients with HNC or the incidence of OSAHS among patients having completed treatment for HNC (ranging from 8% to 95%),2,9,10 rather than a comparison of pretreatment and posttreatment sleep indexes. Furthermore, the majority of the aforementioned studies are affected by diverse anatomical variability with respect to their included HNC cases (including: oral cavity, oropharynx, larynx, and tongue neoplasms), resulting in considerable variability in their respective treatment methods. By contrast, the aim of our study was to assess the effect of radiotherapy and/or chemotherapy treatment on subjective and objective sleep indexes in patients with known NPC and OSAHS.

To our knowledge, there has been only 1 previous publication, a 1981 case report by Moses and Buscemi,11 discussing the association of NPC and SRBD specifically. In that instance, the patient’s presenting symptoms were several months of disabling daytime hypersomnolence, snoring, and intractable hypertension. Obstructive sleep apnea-hypopnea syndrome was not diagnosed via PSG but on the basis of observed apneic episodes despite respiratory effort. Examination of the upper airway with the patient under general anesthesia revealed an obstructing lymphoid mass in the nasopharynx, which was subsequently identified as poorly differentiated epidermoid carcinoma.

Similarly, the chief presenting complaint of one of the patients in our own series was of progressively loud snoring over a 3-month period, which led to a subsequent diagnosis of NPC. In a similar vein to the previous case, this occurrence highlights the need for detailed endoscopic evaluation of the entire upper airway in patients with OSAHS; examinations should not only focus on the severity of hypotonia or hypertrophy of the soft palate and tongue base musculature and PSG results.

It would not be unreasonable to assume that with respect to OSAHS the effect of the treatment of NPC (an obstructing nasopharyngeal mass) might be similar to the effect of the correction of other forms of nasal obstruction. Nasal obstruction is an independent risk factor for OSAHS and is thought to contribute to pharyngeal airway collapse in a number of ways.12 First,
nasal resistance to airflow upstream increases negative pressure in the more collapsible oropharyngeal airway downstream (the Starling resistor model). Second, nasal resistance results in compensatory mouth breathing through the less stable oral airway. Third, decreased nasal airflow decreases stimulation of nasal receptors that help regulate muscle tone and respiratory frequency. And fourth, decreased nasal flow reduces lung nitric oxide levels, with the potential for a ventilation-perfusion mismatch, and negative impacts on pharyngeal muscle tone and arousals. Despite these contributions to the etiology of OSAHS, no direct correlation between degree of nasal obstruction and OSAHS severity has been consistently demonstrated. Furthermore, while multiple studies of both surgical and medical correction of nasal obstruction (for structural causes and perennial allergic rhinitis, respectively) have reported improvements in snoring and subjective sleep quality following treatment, they have failed to consistently demonstrate any improvement in AHI and other indexes related to sleep apnea severity. In fact, the improvements in AHI, mean oxygen saturation, snoring, and ESS observed in our study bear greater resemblance to those in studies of multilevel surgery for OSAHS than to the results of studies of nasal surgery alone. The most likely explanation for this observation is that regional radiotherapy has an effect on other pharyngeal structures involved in the etiology of OSAHS.

A factor central to the discussion of upper airway collapse following radiotherapy is xerostomia. Salivary mucins serve as mucosal lubricants. Surface tension forces associated with mucins play a role in upper airway luminal patency. Therefore, the impairment of mucin production by irradiated salivary glands has the potential to tip the balance in favor of OSAHS. Furthermore, the cicatricial effects of radiotherapy on the upper airway, and on the superior pharyngeal constrictor muscle in particular, may act to pull the tongue posteriorly and decrease the distance between its base and posterior pharyngeal wall. Disturbances of neuromuscular control, impairment of the function of pharyngeal dilator musculature, and the effects on the surrounding tissues of respiratory center may be additional contributing factors. Radiation sinusitis with crusting causing nasal obstruction may increase the likelihood of pharyngeal airway obstruction by the mechanisms previously outlined.

Concepts of surgical treatment for OSAHS are based on reducing the volume of redundant tissues, stiffening the flaccid soft palate, and suspending the collapsed tongue base to maintain airway patency. During the course of our posttreatment follow-up, we observed that all of our patients had a tonsil size of near grade 0 (according the Friedman classification), decreased tongue base size relative to the pretreatment tongue position, and increased cross-sectional area of the airway lumen (per subjective assessment of the examining physician) at 6 months. Theoretically, radiotherapy of the head and neck region will increase the patency of the upper airway by reducing compliance in the surrounding cervical soft tissues. However, despite all patients having received at least local radiotherapy during the course of their treatment, 44% of patients had an increase in AHI after NPC treatment.

The findings of previous studies have been inconsistent with regard to the effect of radiation on OSAHS parameters in patients with HNC. In 2001, Friedman et al reported an OSAHS incidence of 91.7% in 24 patients successfully treated for HNC, including tongue base, pharyngeal, and supraglottic laryngeal tumors. Interestingly, 100% of patients in this series who had received radiation therapy had a posttreatment AHI greater than 15, whereas 78.5% of those who did not receive radiation had an AHI greater than 15. By contrast, in 2010, Qian et al noted that moderate to severe OSAHS was more prevalent in patients with HNC treated with primary surgical resection than in those treated with chemoradiation alone. And in 2009, Steffen et al assessed the prevalence of moderate to severe OSAHS (defined as AHI >20 in their study) among patients treated for HNC (including oral, oropharyngeal, hypopharyngeal, and laryngeal tumors) and found no significant difference in the proportions of patients with or without an AHI greater than 20 who had been treated with radiotherapy. Our results show that the incidence of OSAHS in this small, biased group of patients with NPC was 72%. This is higher than that of the general population.

Interestingly, the fact that mean but not minimum oxygen saturation was improved in our small sample indicates that while the frequency of obstructive events was reduced, their severity was not. This suggestion is supported by the fact that the mean durations of the longest recorded apnea and hypopnea episodes were also unchanged and is a further point of difference from the outcomes of multilevel surgery for OSAHS.

Regarding sleep pattern changes, we found that there was an increase in S1 and S2 phases but a decrease in the deeper stages of sleep in this study. One overlooked probability may be due to xerostomia, which frequently plagues such patients and disturbs their sleep at night. The other factor is systemic chemotherapy itself, which can also affect the central nervous system and potentially affect the central sleep patterns. Conclusions may be difficult from such a small sample, but discussion that these issues were studied for correlation is warranted. Rapid eye movement sleep typically comprises 20% to 25% of total sleep in normal individuals. Obstructive sleep apnea-hypopnea syndrome can result in profound changes in sleep architecture, including suppression of REM and S2, S3, and S4 sleep, with a corresponding increase in S1 sleep. Conversely, the treatment of OSAHS, whether by CPAP or upper airway surgery, has been shown to increase percentage of REM and S2, S3, and S4 sleep, in conjunction with reduction of AHI. In one such study, it was demonstrated that improvement in the respiratory disturbance index with the use of CPAP was significantly correlated with the percentage of REM increase. In another study of the effects of CPAP, increases in percentage of REM and S3 and S4 sleep were linked with subjective improvement of sleep quality. A 2008 meta-analysis of outcomes from multilevel surgery for OSAHS, reported an increase in REM sleep of 44% (weighted average), as well as a 63% reduction in AHI, a 43% reduction in ESS, 63% reduction in snoring VAS score and an 8.8% increase in selected quality-of-life indexes. While improvements in AHI, ESS, and snoring VAS were observed in our patient group, per-
centage of REM, S3, and S4 sleep and sleep efficiency was decreased and percentage of S1 and S2 sleep were significantly increased. Therefore, while symptoms of daytime hypersomnolence were improved, it is possible that subjective sleep quality (which was not formally assessed) may not have improved in these patients following treatment. The assessment of overall quality of life in a group of patients having undergone chemoradiation for NPC is likely to be affected by multiple factors other than sleep quality and, as such, was not formally assessed in this pilot study.

Though sleep apnea was significantly improved in our patient group, our mean posttreatment AHI of 21.7 remained in the category of moderate OSAHs. Our initial recommendation for all patients with posttreatment AHI greater than 15 or AHI greater than 5 with ongoing daytime somnolence was the use of humidified CPAP. Oral appliance therapy was considered an alternative option, though we believed that the common complaint of dry throat with this form of treatment had the potential to be more bothersome in patients with NPC following radiotherapy. Owing to postradiation mucosal changes and the potential for impaired healing, complications following OSAHS surgery may be anticipated. As such, we would be hesitant to suggest aggressive OSAHS surgery for this group of patients. Unfortunately, none of our 14 patients with OSAHS after treatment have continued to use CPAP on a regular basis. Further study of the treatment of patients with both NPC and OSAHS should be conducted, and further refinement of CPAP delivery technology may be warranted.

There were several limitations in this study. First, this was a retrospective study and lacked a control group; Second, the follow-up period was limited to 6 months. Third, the sample size was relatively small. The selection bias and the challenge in knowing absolute incidence of sleep apnea in this pilot study of selected patients with NPC who were predicted to have obstructive sleep apnea was also concerning. Because of this, we hope that this study and results can act as a springboard for future, more comprehensive studies involving patients with NPC. A future study in which all patients with the diagnosis of NPC were analyzed would obviously be the best. Fourth, ESS may lack sensitivity when used as a screening tool for daytime somnolence in the HNC population, since both SRBDs and HNC are likely to affect daytime fatigue. And fifth, despite our focus on the treatment of NPC specifically, variability in the regimens of radiotherapy and chemotherapy delivered should be acknowledged as a possible potential confounder. The T-stage is important because of parapharyngeal extension of these cancers, which will affect the cross-sectional area of the airway, as well as add to the radiation dose to these areas. N-stage is important because the higher tumor load will require higher radiation dose to the neck, thereby also giving a higher dose of radiotherapy to the oropharyngeal airway. Chemotherapy adds to the complications of radiotherapy, such as worsened xerostomia and mucositis. These may worsen the compliance of the pharyngeal wall and secondarily affect sleep. Outcome measures may also be skewed by the treatment process, or the complications from radiotherapy and chemoradiotherapy. However, we are unable to compare the difference between the early and advanced cancer stage because of the relatively low number of patients with NPC with T1 or early T2 stage, who only received radiotherapy in this series. Further studies with long-term follow-up and larger patient numbers would be required to adequately answer these questions.

Conclusions
This pilot study shows a higher percentage of OSAHS in selected patients with NPC. In this study, radiotherapy treatment for patients with NPC improved AHI, snoring severity, and subjective daytime somnolence at 6 months. However, despite these improvements in respiratory parameters, there was a lack of improvement in sleep architecture and ongoing clinically significant OSAHS (necessitating further treatment) in the majority of our patients. Early identification and treatment of OSAHS may be important considerations in the comprehensive management of patients with NPC. Further studies assessing the contribution of these findings to overall patient quality of life are warranted.


