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ORIGINAL ARTICLE

Prevalence of obstructive sleep apnea in patients with squamous cell carcinoma of the tongue following ablation surgery

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KEYWORDS
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Abstract *Background/purpose:* The purpose of this study was to determine the prevalence of obstructive sleep apnea (OSA) in patients with squamous cell carcinoma (SSC) of the tongue after primary surgical resection and to correlate the presence of OSA with the occurrence of obstructive apnea in this patient population.
Materials and methods: This was a retrospective study of 26 Taiwanese patients, 24 males and two females, aged 37–71 years, after surgical resection of SSC of the tongue. Patients who had a follow-up after treatment of 6 months to 11 years were eligible for inclusion. During the post-treatment period, the occurrence of OSA was determined in these patients. Overnight polysomnography (PSG) was used to determine the apnea–hypopnea index (AHI). Patients were considered to have OSA if the AHI value was >5.
Results: Patients with an AHI value of <5 showed a mean body mass index (BMI) of 22.8 kg/m^2, while those with an AHI value of >5 showed a mean BMI of 28.3 kg/m^2. The BMI distribution between patients with AHI value of <5 and those with AHI values of >5 was statistically significant ($P = 0.018$). Using the definition of clinically significant sleep apnea as AHI > 5, 14 of 26 patients (53.85%) had clinical OSA. The OSA and non-OSA groups showed no statistical significance in terms of age, tumor size, tongue ablation, neck dissection [method?], or wound reconstruction methods.
Conclusion: Incidence of OSA in the patient population with SSC of the tongue was found to be significantly higher than that in the general population. The limitations of this study were the

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relatively small patient sample size and no presurgical PSG record being obtained from the patients to compare the sleep quality before and after cancer therapy.

Introduction

Obstructive sleep apnea (OSA) is a chronic condition characterized by frequent episodes of upper airway collapse during sleep. It is associated with severe daytime hypersomnolence, cardiovascular diseases such as systemic hypertension and arrhythmias, and automobile accidents, thereby resulting in significant morbidity and mortality. The prevalence of OSA is approximately 2% in women and 4% in men in the general population.[1] Furthermore, a study of sleep-disordered breathing (SDB) using full polysomnography (PSG) demonstrated a high prevalence of OSA syndrome (OSAS) of 8.8% among Chinese middle-aged male office-based workers in Hong Kong [apnea—hypopnea index (AHI) of $\geq$5 plus excessive daytime sleepiness].[2]

Factors that increase the vulnerability of OSA include age, gender, obesity, family history, menopause, craniofacial abnormalities, and certain health behaviors such as cigarette smoking and alcohol abuse.[1,3] Although craniofacial abnormalities have an effect on patients with OSA, these significantly vary among patients with (1) enlarged soft tissues such as the tongue base and palate,[4,5] (2) narrowing of the pharyngeal space due to anatomic abnormalities,[6,7] and (3) loss of function of the pharyngeal space due to anatomic abnormalities.[8] Thus, patients who were successfully treated for head and neck cancers often have a partially obstructed upper airway, which is functional during the day but collapses during sleep.[9,10] Some case reports of head and neck cancers also suggested that these patients may subsequently develop OSA following either surgical or radiation treatment.[11—15] However, since the head and neck region has broad anatomical coverage and includes the lips, oral cavity, nasal cavity, paranasal sinuses, pharynx, and larynx, these case reports did not pinpoint the specific anatomical area that might influence the development of OSA.

In Taiwan, oral cancer is the fourth predominant cancer among males, while the tongue region is one of the high-prevalence areas affected by oral squamous cell carcinoma (SSC). Most patients with surgically treated tongue cancer were also documented to have a narrow upper airway with a high incidence of OSA.[16] Narrowing of the upper airway as a result of surgery may be due to immobile and bulky flap reconstructions, altered suprahyoid and pharyngeal musculature, soft-tissue fibrosis, etc.[17] Theoretically, radiotherapy may have both beneficial and detrimental effects on the upper airway. In some cases, radiotherapy may cause tissue scarring that contracts and narrows the airway, thereby causing OSA to develop. In other cases, radiation may have a beneficial effect of tightening redundant soft tissue in the upper airway or reducing excessive tongue base tissue, thereby decreasing the likelihood of OSA.[8]

Literature reviews seldom reported correlations or prevalence of OSA after tongue-cancer surgery. This preliminary pilot study was initiated to determine the prevalence of OSA in a select group of patients with primary SSC of the tongue who underwent resection with different reconstruction and/or radiotherapeutic techniques using PSG and to compare them with the general population.

Materials and methods

Participants

This was a retrospective cross-sectional study of the prevalence of patients with sleep apnea who suffered from primary SSC of the tongue and had been treated with ablation surgery. Patients with cancer that involved other areas such as the pharynx or larynx were excluded from the study. Furthermore, patients who underwent a total laryngectomy, those who were breathing with the assistance of a tracheotomy/tracheostomy, or those with obstructive pulmonary disease or a history of OSA prior to the operation were not included in the study.

Twenty-six patients who underwent surgery with or without radiotherapy of the tongue SSC were recruited from the Division of Oral and Maxillofacial Surgery of Taichung Veterans General Hospital. Data were collected during January—April 2009. Types of tongue surgery included wide excision and a hemiglossectomy to a nearly total glossectomy. The ablated tongue was reconstructed with a skin graft, pedicle, or free flap, while neck surgeries included suprahyoid, modified, and radical neck dissection. Patients with post-treatment follow-up of 6 months to 11 years and who were free of any residual or recurrent disease were eligible for inclusion. The following variables were recorded for each participant: age (years), gender, weight (kg), body height (cm), BMI (defined as the patient's weight divided by the square of the patient's height; kg/m^2), substance use (alcohol, smoking, or betel quid chewing), tumor size, glossectomy, neck dissection, reconstruction, and radiotherapy (Tables 1 and 2).

Sleep studies

In the post-treatment period, a sleep study was performed using overnight PSG, including electroencephalography, electrocardiography, electroculography, submental electromyography, airflow, nasal and oral breathing monitored with a thermocouple, chest and stomach breathing movements monitored with a pressure-sensitive belt, body movements, blood saturation monitored with a pulse oximeter, and loudness of snoring monitored with a decibel meter at a distance of 1 m.[18] PSG data were downloaded into

Table 1 Baseline characteristics and PSG results of patients.

Participant	Gender	Age	BMI	Lowest SpO_2	Obstructive apnea	Hypopnea	AHI	Tumor size (cm)	Glossectomy	Neck dissection	Reconstruction	Radio-therapy
1	Male	32	23.94	93	0	4	0.6	2	Partial	Suprahyoid	STSG	0
2	Male	52	29.24	91	0	1	0.7	3	Partial	Nil	STSG	0
3	Male	50	27.12	90	3	0	4.2	2	Partial	Radical	STSG	0
4	Male	32	20.93	93	0	0	0	2	Partial	Suprahyoid	PMMC	1
5	Male	60	22.50	94	0	0	0	4	Partial	Radical	PMMC	1
6	Male	71	19.14	90	0	5	1	3	Hemi	Radical and suprahyoid	STSG	1
7	Male	56	24.57	91	9	8	4	2	Hemi	Suprahyoid	Free flap	1
8	Male	59	20.08	93	1	14	3	1	Partial	Radical and suprahyoid	STSG	1
9	Male	47	22.57	91	0	5	0	2	Hemi	Suprahyoid	STSG	1
10	Male	44	18.59	95	0	1	0	3	Hemi	Radical	STSG	1
11	Male	49	20.03	93	0	0	0	3	Hemi	Radical	STSG	1
12	Male	48	24.78	90	5	7	2.6	2	Partial	Suprahyoid	STSG	1
13	Male	52	22.53	90	6	31	5.8	1	Partial	Nil	STSG	0
14	Male	59	26.58	85	6	0	5.9	1	Partial	Radical	PMMC	0
15	Female	40	24.03	90	5	12	7.8	3	Hemi	Nil	STSG	0
16	Male	42	24.45	84	6	54	10.6	1	Partial	Radical	STSG	0
17	Male	46	26.21	86	1	32	5.8	3	Partial	Suprahyoid	STSG	1
18	Male	49	23.99	90	11	27	10	2	Partial	Radical and suprahyoid	Free flap	1
19	Male	56	27.13	86	9	67	14.8	4	Partial	Radical	STSG	1
20	Male	54	28.46	72	0	148	25.6	3	Hemi	Suprahyoid	Free flap	1
21	Male	66	29.67	80	64	113	44.4	4	Hemi	Nil	STSG	1
22	Male	48	29.41	84	4	120	24.1	3	Partial	Radical	Free flap	0
23	Male	50	36.75	80	5	157	27.1	3	Partial	Radical	STSG	0
24	Male	71	28.29	83	3	36	8.2	5	Hemi	Suprahyoid	STSG	1
25	Male	61	24.88	89	43	13	11.8	4	Hemi	Radical	Free flap	1
26	Female	59	29.23	88	26	56	15	4	Total	Bilateral modified	Free flap	1

AHI = apnea—hypopnea index; BMI = body mass index; PMMC = pectoralis major myocutaneous flap; SpO2 = pulse oximetry oxygen saturation; STSG = split thickness skin graft.

the computer for further interpretation. PSG records were manually scored. An abnormal breathing event (obstructive apnea) during objectively measured sleep was defined according to commonly used clinical criteria of a cessation of airflow for at least 10 seconds. The event was obstructive if, during the apnea, there was an effort to breathe. An abnormal respiratory event (hypopnea) was defined as at least a 30% reduction in the thoracoabdominal movement or airflow compared to the baseline lasting for at least 10 seconds, with $\geq$4% oxygen desaturation. The average number of episodes of apnea and hypopnea per hour of sleep (AHI) was calculated as a summary measurement of OSA.[1] Patients were considered to have OSA if the AHI value was $>$5.[17]

Data analysis

Traditional statistical analyses using $\chi^2$and Fisher exact tests were used to compare the test results of tongue-cancer patients with those of OSA sufferers in a normal population. All analyses were done with statistical software (Statistical Package for the Social Sciences, ver. 11.0 for Windows; SPSS, Chicago, IL, USA).

Results

There were 26 Taiwanese patients (24 males and two females) with SSC of the tongue after surgical resection who participated in this study. Their ages ranged from 32 to 71 (mean, 52) years, and BMI from 18.9 to 36.75 (average, 25.2) kg/m^2. Fifteen of 26 patients had a BMI of $<$25 (average, 22.5) kg/m^2, while the remaining 11 patients had a BMI of $>$25 (average, 28.9) kg/m^2 (Table 1). In the group ($n = 12$) with an AHI of $<$5, the mean BMI was 22.8 ± 3.3 kg/m^2, while in the group ($n = 14$) with an AHI of $>$5, the mean of BMI was 26.3 ± 3.8 kg/m^2. The BMI

Table 2 Correction of OSA with baseline data, oral habits, and treatment.

	AHI < 5 (n = 12)			AHI ≥ 5 (n = 14)			P
	Median	25th percentile	75th percentile	Median	25th percentile	75th percentile	
Age	49.50	44.75	58.25	57.50	49.75	61.25	0.085
BMI	22.54	20.04	24.72	25.86	23.33	28.52	0.017
Obstructive apnea	0.00	0.00	2.50	6.00	3.75	14.75	0.001
Hypopnea	2.50	0.00	6.50	45.00	23.50	114.75	<0.001
Tumor size	2.50	2.00	3.00	3.25	1.88	4.00	0.274
	n (%)			n (%)			
Alcoholic drinking							
No	6 (54.5)			6 (60.0)			1.000
Yes	5 (45.5)			4 (40.0)			
Betel nut chewing							
No	2 (18.2)			3 (30.0)			0.635
Yes	9 (81.8)			7 (70.0)			
Cigarette smoking							
No	3 (27.3)			2 (20.0)			1.000
Yes	8 (72.7)			8 (80.0)			
Radiotherapy							
No	3 (25.0)			6 (42.9)			0.429
Yes	9 (75.0)			8 (57.1)			
Neck operation							
No	1 (8.3)			3 (21.4)			0.598
Yes	11 (91.7)			11 (78.6)			

Mann–Whitney *U* test, significant at P < 0.05.
AHI = apnea–hypopnea index; BMI = body mass index; OSA = obstructive sleep apnea (OSA).

distribution between patients with an AHI of <5 and those with an AHI of >5 was statistically significant (P = 0.018).

The AHI ranged from 0 to 44.4 (average, 8.96). Using the definition of clinically significant sleep apnea as an AHI of >5 or a minimum oxygen desaturation of <90%, 14 of 26 patients (53.85%) were found to have clinical OSA. The lowest oxygen saturation found in this study was 72%. As to the age parameter, the group with an AHI of <5 had a mean age of 50 years, and that with an AHI of >5 had a mean age of about 57 years, which was not statistically significant (P = 0.085) (Tables 1 and 2).

The mean size of the SSC primary tumor of the tongue was about 2.7 cm in diameter (Table 1). There was no statistically significant difference between the group with an AHI of <5 and that with an AHI of >5 (P = 0.274). Among all patients, 85% underwent neck dissection. Using different neck dissection methods in treating the tongue cancer revealed no statistical significance (P = 0.598) (Table 1). Seventeen of 26 patients (65.4%) received radiation therapy; eight (47.06%) of those patients had an AHI of >5. In the non-radiation therapy group, six of nine (66.7%) patients had an AHI of >5, which was not statistically significant (P = 0.429) (Table 1). The OSA and non-OSA groups also showed no statistically significant differences in terms of tongue ablation or wound reconstruction methods.

Discussion

The prevalence of OSA in patients with SSC of the tongue was 53.85% and was determined to be significantly higher than that of the general population (3–7% for adult men and 2–5% for adult women).[1] It was also 6.1 times higher than that of male Chinese middle-aged office-based workers in Hong Kong with OSAS (AHI ≥5 and excessive daytime sleepiness) at 8.8%.[2] This clearly shows that the incidence of OSA in tongue-cancer patients is extremely high compared to that of the general population. In a study of 16 tongue-cancer patients, only one was diagnosed with OSA.[17] The prevalence of OSA of tongue-carcinoma patients after treatment in this study was also much higher than that in studies conducted in other countries.

However, OSA and non-OSA patients showed no statistically significant differences in terms of age, snoring index, tumor size, neck dissection, type of tongue reconstruction, or response to radiotherapy, but did so for the BMI (P = 0.018). In fact, a high BMI was clearly demonstrated to be a significant risk factor for OSA (Tables 1 and 2). A higher BMI (26.3 ± 3.8 kg/m^2) was more frequently seen in the tongue-cancer patients with OSA than in non-OSA patients (22.8 ± 3.3 kg/m^2). Since the average BMI in this study (25.2 kg/m^2) was higher than that in the study conducted by Ip et al[2] (23.9 kg/m^2), the higher incidence of OSA might have been due to the higher BMI rather than due to tongue cancer only.

The incidence of OSA in tongue-cancer patients, particularly its relationship with the various treatment modalities, remains unclear and is still poorly defined. Nevertheless, it is reasonable to assume that patients who have undergone treatment for tongue cancer with or without flaps to replace the cancerous tongue tissue may experience OSA. However, a limitation of this study was that the patient sample size was insufficient to evaluate the direct influences of age, snoring index, tumor size, local recurrence, neck lymph node metastasis, neck dissection, and radiotherapy (radiated vs. nonradiated) on OSA (Tables 1 and 2). Furthermore, no presurgical PSG was recorded. Therefore, whether tongue cancer itself or the consequences of tongue ablation surgery, flap reconstruction, radiotherapy, or chemotherapy induced or worsened OSA cannot be answered in this study. It is suggested that healthcare providers monitor the sleep quality of tongue-cancer patients before and after cancer therapy.

In this study, the "gold standard" diagnostic test of overnight PSG is an ideal method for assessing the prevalence of OSA in post-treatment tongue-cancer patients. Moreover, it would be ideal if tongue-cancer patients were assessed by overnight PSG prior to undergoing treatment, to determine the preexistence of OSA. Pre- and post-treatment analyses of OSA in tongue-cancer patients are required to demonstrate any significant level of association between the treatment type and the sleep apnea status.

Treatment for tongue cancer has evolved over the past 100 years. Nowadays, aside from continual improvements in surgical techniques such as tumor resection and free flap reconstruction, the quality of sleeping well without apnea should be considered in modern-day cancer therapy. The identification and treatment of OSA might be important factors in improving the quality of life of tongue-cancer patients.

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