Characteristics of Nonsmokers Under 50 years old with Oral Cavity Cancer

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ABSTRACT

Introduction
Oral cavity squamous cell carcinoma (OCSCC) has traditionally been thought of as a disease in older patients with a history of tobacco, alcohol, or betel nut use. More recently studies have discussed OCSCC in nonsmoker populations and in younger populations, however research lacks in combination of the groups.

Methods
After Institutional Review Board approval, a retrospective chart review was conducted on patients diagnosed with OCSCC at the age of 50 years old or younger. Patients were divided based on tobacco or betel nut exposure for 0-5 years and 5+ years.

Results
There were 121 patients that met criteria, 8 of which were excluded given lack of care records available beyond initial consultation. There were 38 patients (34%) who never had any tobacco exposure and 8 (7%) with less than 5 pack year history or 5 year history of betel nut use. The remaining 67 (59%) are current tobacco or betel nut users or prior users with a significant tobacco history. Within the limited or no tobacco exposure group, the average age was 42 years old with 27 patients (59%) presenting with a T1 or T2 lesion and 27 (63%) that were clinically or pathologically N0. The average follow up with 4.2 years with 11 patients (24%) with local or regional recurrence and 6 patients (13%) dying of their disease. The group with notable tobacco or betel nut exposure had an average age of 45 with 46 patients (69%) presenting with a T1 or T2 lesion and 45 (67%) that were clinically or pathologically N0. The average follow up was 4.3 years with 16 patients (24%) having persistence or local recurrent and 9 (13%) dying of their disease. There was no difference in any pathologic characteristics, recurrence, or distant-free or overall survival. The limited exposure or nonsmoker group were significantly younger and had a different race distribution and trended toward more females, but did not reach significance.

Conclusions
Our data does not support a more aggressive disease course in young patients with limited exposures. This unique entity should be further studied to attempt to determine what causes OCSCC in this population.

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INTRODUCTION

Oral cavity squamous cell carcinoma (OCSCC) related to alcohol, tobacco, and betel nut use has long been studied and the relationship well understood. Chronic exposure to these toxins is closely linked to OCSCC and often seen in older patients after years of exposure. Studies have shown the nonsmoker nondrinker population is predominantly females in their 60-80s with no more aggressive disease and similarly disease free survival (DFS) as the smoking and drinking population.

However, more recently there is an increased incidence of oral cavity cancer in younger patients. Unlike in oropharyngeal carcinoma, this does not appear to be HPV mediated. Additionally, these patients may nature of their age have had less years of exposures if any. Prognosis on this population is controversial, however data overall does not suggest a more aggressive disease or decreased DFS.

While there is data to independently comment on these two unique populations, research lacks in understanding the prognosis and characteristics of nonsmoker young patients

We hypothesis that nonsmoker young patients have more aggressive pathologic disease and have decreased disease-free survival.

METHODS AND MATERIALS

After receiving Institutional Review Board approval, a retrospective chart review was conducted. Patients were pulled via ICD-10 codes for malignant neoplasm oral cavity cancer of all subsites from January 2007 to October 2022.

Included if:
- biopsy proven OCSCC
- 50 years old or younger at time of diagnosis
- followed beyond initial diagnosis

Definitions:
NONSMOKER: limited (<5 pack year history) tobacco exposure or betel nut use. None had significant alcohol use
SMOKER: history of 5+ pack year tobacco exposure or betel nut use

RESULTS

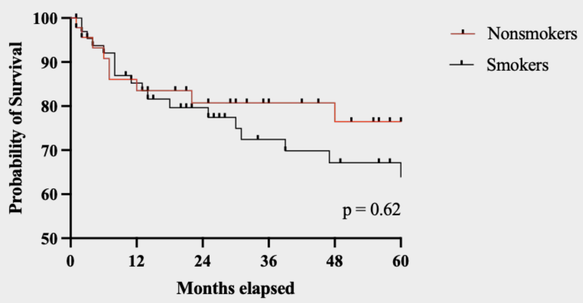
DEMOGRAPHICS

	Nonsmokers n=46		Smokers n=67		
	n	***%***	***n***	***%***	
Sex					p=0.06
Male	27	59	51	76	
Female	19	41	16	24	
Age *					**p=0.02**
Average	42		45		
Min	26		25		
Max	50		50		
Race *					**p=0.04**
Black	0	0	2	3	
Hispanic	4	9	1	1	
White	38	83	48	72	
Other	4	9	16	24	
Comorbities					
Autoimmune disease	6	13	9	13	p=1.00
DM	3	7	4	6	p=1.00
HTN	9	20	14	21	p=1.00
Prior malignancy	3	7	10	15	p=0.23
Obesity	18	39	20	30	p=0.32
OSA	3	7	2	3	p=0.40
Follow up (years)	4.2		4.3		p=0.72

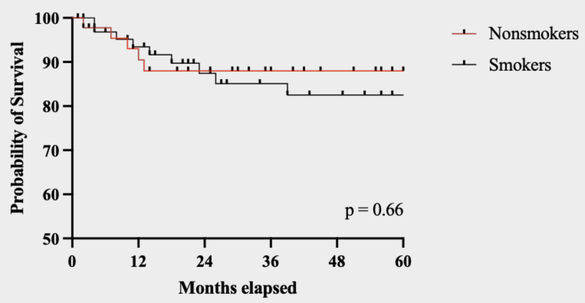
PATHOLOGIC CHARACTERISTICS

	Nonsmokers n=46		Smokers n=67		
	n	***%***	***n***	***%***	
Tumor Stage					p=0.32
T1/T2	27	59	46	69	
T3/T4	19	41	21	31	
Nodal Disease					p=0.43
N0	27	63	45	67	
N1+	19	41	22	33	
PNI	17	37	18	27	p=0.30
ECE					
Yes	9	20	13	19	p=1.00
No	30	65	44	66	
Locoregional Recurrence	11	24	16	24	p=1.00

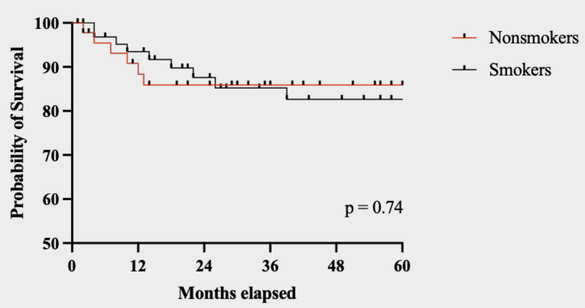
Recurrence



Disease-free Survival



Overall Survival



DISCUSSION

Young patients with limited exposure to alcohol, tobacco, and betel nut make up a unique subset of patients in those with OCSCC. Unlike in oropharyngeal cancer, there is not a known cause such as HPV status.

In our cohort, we saw a significant difference in age with nonsmoker or limited exposure cohort being 3 years younger on average and with the distribution of race. There were more females in the limited exposure group, however this did not reach significance.

There was no significant difference in pathologic characteristics, recurrence, or disease-free/overall survival.

The data is mixed regarding OCSCC in younger patients and in patients with limited exposure. A large meta-analysis from Lee et al found no difference in survival amongst young and old patients with OCSCC with the age cut off of 40 years old. Another database search reviewing 26 articles found that most of the patients with limited exposures who developed OCSCC were in their 8th decade and had comparable survival rates to their counterparts with exposure to known toxins. Literature overall agrees with these larger studies. However, the group of young nonsmokers who develop OCSCC is not as well covered. One study with 49 patients suggested a worse overall survival outcome in the patients under 45 year old with 10 years or less of exposures compared to 10+ years of exposures. This is a very limited sample and does not address disease-specific survival. Specifically in this group, neither subset has many years of exposures to toxins or other chronic medical conditions with systemic inflammatory effects. There was no difference in the comorbidities between the groups. While OCSCC in young nonsmokers appears to behave similarly to that in young smoker patients, it appears to be a separate entity. The data does not support more aggressive treatment, but further investigation into what is the cause.

CONCLUSIONS

OCSCC in young patients is a unique entity, and even more specifically, when it appears in nonsmokers or those with limited exposures. It does not appear to be more aggressive of a disease process based on pathologic characteristics, recurrence, or survival. The nonsmoker group has more women of white and hispanic races and were younger compared to their counterparts with exposures. They should not be treated outside of the normal treatment algorithm or receive more aggressive treatment.Further studies are needed to explore the possible etiology in young patients with OCSCC with limited exposures.

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