

Clinical characteristics of low-risk patients developing oral cavity cancer

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Background

- Oral cavity cancer (OCC) is the 6th most common malignancy in the world, with over 800,000 new cases diagnosed each year
- Among head and neck cancers, OCC accounts for more than 30% of cases
- While there are specific risk factors for OCC such as tobacco and alcohol use, at least 15-20% of patients with OCC lack any known risk factor

Purpose

- To identify and describe the clinical and environmental factors affecting the low-risk OCC population that may predispose them to this malignancy
- Analyze and determine if these differences are statistically significant from the typical OCC population

Methods and Study Design

- This retrospective clinical chart review targeted 501 patients that had been diagnosed with squamous cell carcinoma of the oral cavity from 2012-2019 and were treated at the James Cancer Hospital and Solove Research Institute
- Low risk cohort was defined as non-smokers and non-drinkers or non-smokers and <14 drinks per week. High risk cohort was anyone else.
- Patient characteristics were compared between these groups using Chi-square test or fisher exact test for the categorical variables, and Kruskal-Wallis test for the continuous variables. P-values < 0.05 were deemed to be statistically significant

Data

Demographic Summary by cohort					
Variable		1:non-smokers and non-drinkers or non-smokers and <14 drinks (n=160)	2:anyone else (n=341)	Total (n=501)	p-value
Age	Median [IQR] (min, max)	66 [54, 73.5] (13, 91)	62 [54, 70] (27, 93)	63 [54, 71] (13, 93)	0.1882
BMI	Median [IQR] (min, max)	26.5 [22.7, 32.6] (14.9, 62)	24 [20.7, 28.3] (12.8, 89.6)	25.1 [21.2, 29.5] (12.8, 89.6)	0.0001
Gender	1:Male	67 (41.9%)	237 (69.5%)	304 (60.7%)	<0.001
	2:Female	93 (58.1%)	104 (30.5%)	197 (39.3%)	
Race	Missing	13 (8.1%)	42 (12.3%)	55 (11%)	0.0031
	1:White	135 (84.4%)	281 (82.4%)	416 (83%)	
Obesity	2:Black	3 (1.9%)	15 (4.4%)	18 (3.6%)	0.1244
	3:Other	9 (5.6%)	3 (0.9%)	12 (2.4%)	
	1:No	112 (70%)	283 (83%)	395 (78.8%)	0.0009
	2:Yes	48 (30%)	58 (17%)	106 (21.2%)	

Table 1: Patient demographics

Past medical history characterization by cohort				
Variable		1:non-smokers and non-drinkers or non-smokers and <14 drinks (n=160)	2:anyone else (n=341)	Total (n=501)
Diabetes	1:No	119 (74.4%)	272 (79.8%)	391 (78%)
	2:Yes	41 (25.6%)	68 (19.9%)	109 (21.8%)
HTN	1:No	58 (36.3%)	134 (39.3%)	192 (38.3%)
	2:Yes	102 (63.8%)	206 (60.4%)	308 (61.5%)
Hypothyroidism	1:No	117 (73.1%)	285 (83.6%)	402 (80.2%)
	2:Yes	43 (26.9%)	55 (16.1%)	98 (19.6%)
CAD	1:No	140 (87.5%)	272 (79.8%)	412 (82.2%)
	2:Yes	20 (12.5%)	68 (19.9%)	88 (17.6%)
CHF	1:No	156 (97.5%)	317 (93%)	473 (94.4%)
	2:Yes	4 (2.5%)	23 (6.7%)	27 (5.4%)
CVS	1:No	149 (93.1%)	309 (90.6%)	458 (91.4%)
	2:Yes	11 (6.9%)	31 (9.1%)	42 (8.4%)
PVD	1:No	155 (96.9%)	310 (90.9%)	465 (92.8%)
	2:Yes	5 (3.1%)	30 (8.8%)	35 (7%)
COPD	1:No	158 (98.8%)	256 (75.1%)	414 (82.6%)
	2:Yes	2 (1.3%)	84 (24.6%)	86 (17.2%)
Hx of autoimmune dz	1:No	146 (91.3%)	328 (96.2%)	474 (94.6%)
	2:Yes	14 (8.8%)	12 (3.5%)	26 (5.2%)
Hx of immunodeficiency	1:No	157 (98.1%)	340 (99.7%)	497 (99.2%)
	2:Yes	3 (1.9%)	0 (0%)	3 (0.6%)
Diabetes + Obesity	1: No	144 (90%)	321 (94.1%)	465 (92.8%)
	2: Yes	16 (10%)	19 (5.6%)	35 (7%)

Table 2: Past Medical History characterization

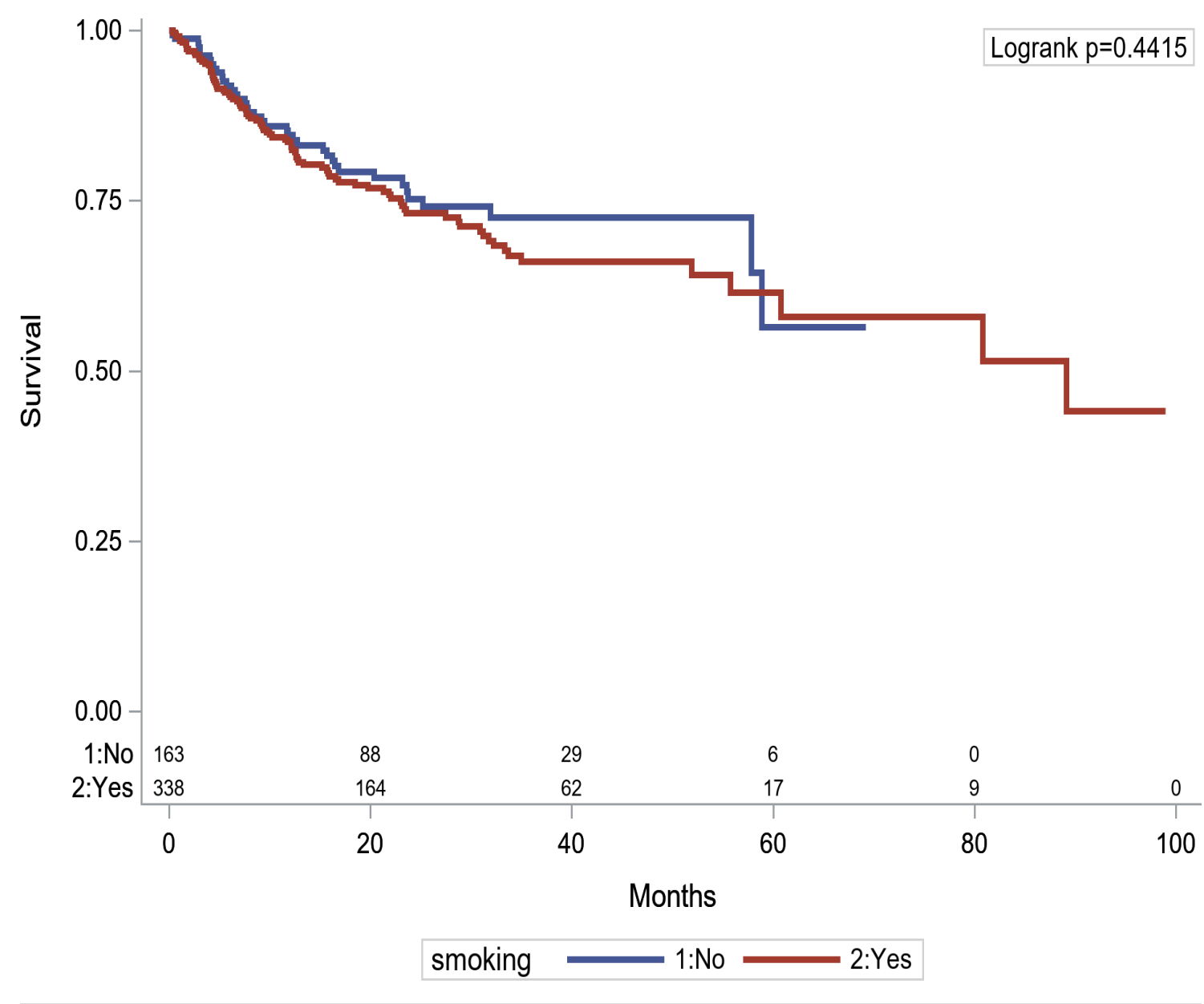


Figure 1: Kaplan Meier Curve of Overall Survival by smoking status

Pathologic characterization by cohort				
Variable		1:non-smokers and non-drinkers or non-smokers and <14 drinks (n=160)	2:anyone else (n=341)	Total (n=501)
Tumor size (cm)	Median [IQR] (min, max)	2.7 [1.5, 4.3] (0, 10.2)	2.9 [1.6, 4.3] (0.1, 10.8)	2.9 [1.6, 4.3] (0, 10.8)
				0.3660
Tumor Volume (cm3)	Median [IQR] (min, max)	9 [3.1, 26.9] (0.2, 442)	8.3 [2.4, 32] (0, 615)	8.5 [2.7, 31.3] (0, 615)
				0.9358
Tumor Differentiation	1:Poor	16 (10%)	21 (6.2%)	37 (7.4%)
	2:Moderate	82 (51.3%)	189 (55.4%)	271 (54.1%)
	3:Well	48 (30%)	115 (33.7%)	163 (32.5%)
Lymphovascular invasion	1:No	106 (66.3%)	230 (67.4%)	336 (67.1%)
	2:Yes	42 (26.3%)	92 (27%)	134 (26.7%)
Perineural Invasion	1:No	64 (40%)	144 (42.2%)	208 (41.5%)
	2:Yes	84 (52.5%)	180 (52.8%)	264 (52.7%)
Lymph nodes examined	Median [IQR] (min, max)	missing=9 31 [17, 48] (0, 132)	missing=13 34 [19, 51.5] (0, 132)	missing=22 33 [18, 51] (0, 132)
				0.2751
Depth of invasion	Median [IQR] (min, max)	missing=14 0.9 [0.5, 1.9] (0, 8)	missing=41 1.2 [0.5, 2.2] (0.1, 6.8)	missing=55 1.1 [0.5, 2] (0, 8)
				0.0386
Extracapsular spread	Missing	16 (10%)	34 (10%)	50 (10%)
	1:No	118 (73.8%)	255 (74.8%)	373 (74.5%)
Type of node	2:Yes	26 (16.3%)	52 (15.2%)	78 (15.6%)
	Missing	96 (60%)	205 (60.1%)	301 (60.1%)
	1:Macro	48 (30%)	91 (26.7%)	139 (27.7%)
	2:Micro	16 (10%)	45 (13.2%)	61 (12.2%)
T Stage	1	49 (30.6%)	92 (27%)	141 (28.1%)
	2	43 (26.9%)	76 (22.3%)	119 (23.8%)
	3	22 (13.8%)	55 (16.1%)	77 (15.4%)
N Stage	0	68 (42.5%)	146 (42.8%)	214 (42.7%)
	1	20 (12.5%)	46 (13.5%)	66 (13.2%)
	2	40 (25%)	81 (23.8%)	121 (24.2%)
M Stage	3	68 (42.5%)	146 (42.8%)	214 (42.7%)
	Missing	6 (3.8%)	7 (2.1%)	13 (2.6%)
	0	154 (96.3%)	334 (97.9%)	488 (97.4%)

Table 3: Pathologic characterization

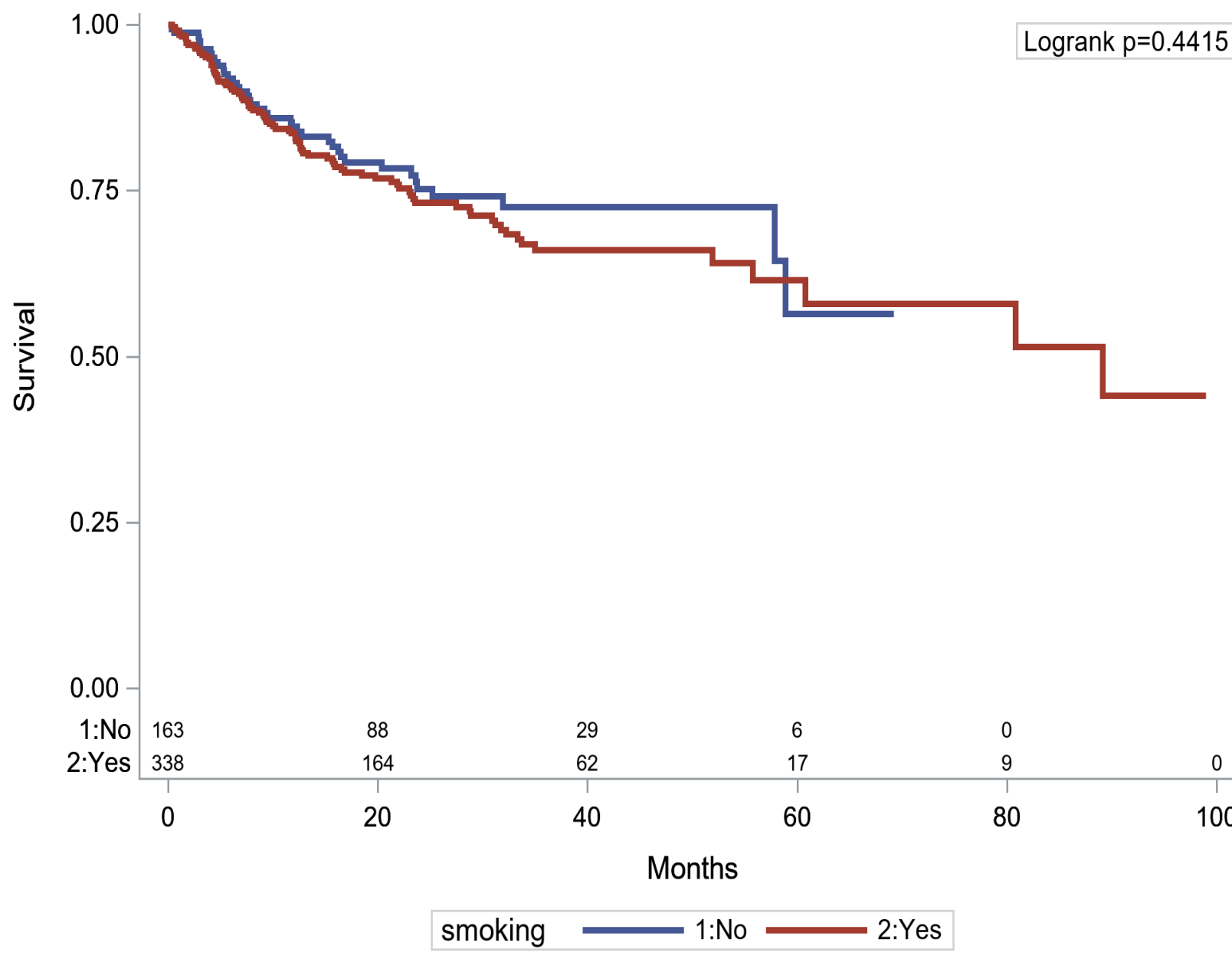


Figure 2: Kaplan Meier Curve of Disease-free survival by smoking status

Univariate overall survival and disease-free analysis			
Overall survival	1:Low-risk cohort–Ref	.	0.4011
	2:Anyone else	1.18 (0.81, 1.72)	.
Disease free survival	1:Low-risk cohort–Ref	.	0.3527
	2:Anyone else	0.87 (0.56, 1.36)	.

Table 4: Univariate overall survival and disease-free analysis

Results

- The low-risk OCC cohort constituted approximately 32% of our entire patient population
- Demographics of the low-risk population were overwhelmingly female (58.1%), whereas the high-risk population was overwhelmingly male (69.5%)
- The prevalence of obesity, hypothyroidism, a history of immunodeficiency, and auto-immune disease was significantly increased in the low-risk population
- Tumor pathology between the two cohorts was extremely similar with tumor size, perineural/lymphovascular invasion, tumor differentiation, LN involvement, and tumor staging all being comparable except for depth of invasion which was higher in the high-risk cohort
- Smoking and drinking status did not affect disease-free survival or overall survival which demonstrates that lack of classic OCC risk factors does not confer an advantage in clinical progression
- Kaplan Meier curves for both overall survival as well as disease-free survival by smoking status show no significant differences
- Univariate overall survival as well as disease-free survival showed no significant differences between the low and high-risk cohorts

Conclusions

We have identified a cohort of patients that are at risk of developing oral cavity cancer, despite lack of typical risk factors. The phenotype of this cohort is predominantly white women with a significant history of autoimmune disease, immunodeficiency, hypothyroidism, and obesity. Despite lack of traditional risk factors, the cancer in this low-risk cohort has the same pathology and clinical outcome as the high-risk cohort. With no known risk factors in this patient population, our findings are interesting and warrant more investigation into the role of inflammatory processes and immunocompromised states in the role of OCC development.

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