

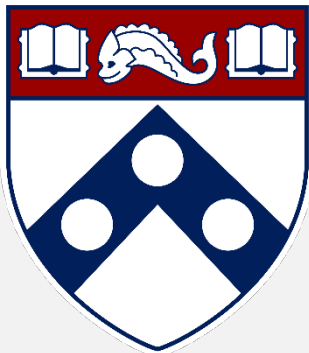


Nodal Disease Status and Treatment Trends for Oral Cavity Squamous Cell Carcinoma; A National Cancer Database Review

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Introduction

The oral cavity is comprised of multiple, distinct anatomic subsites including the mucosal lip, oral tongue, alveolar ridge, floor of mouth, hard palate, buccal mucosa, and retromolar area. Squamous cell carcinoma (SCC) makes up nearly 90% of all primary oral cavity cancer and can originate from the squamous mucosal lining within any of these unique subsites¹. The American Joint Committee on Cancer (AJCC) staging system recognizes these unique anatomical sites within the oral cavity, but does not delineate between them for the purposes of cancer staging and treatment recommendations². There are differences in the rates of occult nodal disease and presentation for different oral cavity subsites which have not been fully described.

The purpose of this study is to use the National Cancer Center Database (NCDB) to further analyze rates of regional nodal metastasis and management of the neck for each of the oral cavity SCC subsites.

Study Design and Measures

This is a retrospective population-based cohort study of patients in the National Cancer Database (NCDB) diagnosed with non-metastatic oral cavity SCC between January 2004 and December 2016 who underwent surgery with neck dissection.

Oral cavity SCC patients were divided into primary tumor sites which included mucosal lip, oral tongue, alveolar ridge, floor of mouth, hard palate, buccal mucosa, and retromolar area.

Lip:						Retromolar area:					
	level	T1	T2	T3	T4		level	T1	T2	T3	T4
n		203	114	34	38	n		249	407	110	595
NODAL_DISEASE (%)	cN+ & pN+	4 (2.0)	17 (14.9)	10 (29.4)	11 (28.9)	NODAL_DISEASE (%)	cN+ & pN+	46 (18.5)	123 (30.2)	40 (36.4)	255 (42.9)
	cN+ & pN0	3 (1.5)	5 (4.4)	7 (20.6)	5 (13.2)		cN+ & pN0	7 (2.8)	25 (6.1)	15 (13.6)	65 (10.9)
	cN0 & pN+	4 (2.0)	9 (7.9)	3 (8.8)	2 (5.3)		cN0 & pN+	31 (12.4)	72 (17.7)	17 (15.5)	73 (12.3)
	cN0 & pN0	192 (94.6)	83 (72.8)	14 (41.2)	20 (52.6)		cN0 & pN0	165 (66.3)	187 (45.9)	38 (34.5)	202 (33.9)
Tongue:						Floor of Mouth:					
	level	T1	T2	T3	T4		level	T1	T2	T3	T4
n		4844	4586	1280	830	n		1453	1619	424	1822
NODAL_DISEASE (%)	cN+ & pN+	440 (9.1)	1139 (24.8)	614 (48.0)	500 (60.2)	NODAL_DISEASE (%)	cN+ & pN+	234 (16.1)	450 (27.8)	193 (45.5)	871 (47.8)
	cN+ & pN0	101 (2.1)	281 (6.1)	118 (9.2)	87 (10.5)		cN+ & pN0	39 (2.7)	114 (7.0)	50 (11.8)	230 (12.6)
	cN0 & pN+	529 (10.9)	949 (20.7)	240 (18.8)	103 (12.4)		cN0 & pN+	119 (8.2)	226 (14.0)	59 (13.9)	199 (10.9)
	cN0 & pN0	3774 (77.9)	2217 (48.3)	308 (24.1)	140 (16.9)		cN0 & pN0	1061 (73.0)	829 (51.2)	122 (28.8)	522 (28.6)
Alveolar Ridge:						Hard Palate:					
	level	T1	T2	T3	T4		level	T1	T2	T3	T4
n		569	646	143	1690	n		98	127	58	251
NODAL_DISEASE (%)	cN+ & pN+	64 (11.2)	119 (18.4)	39 (27.3)	528 (31.2)	NODAL_DISEASE (%)	cN+ & pN+	18 (18.4)	36 (28.3)	20 (34.5)	91 (36.3)
	cN+ & pN0	12 (2.1)	38 (5.9)	15 (10.5)	210 (12.4)		cN+ & pN0	3 (3.1)	2 (1.6)	3 (5.2)	33 (13.1)
	cN0 & pN+	40 (7.0)	90 (13.9)	15 (10.5)	165 (9.8)		cN0 & pN+	2 (2.0)	16 (12.6)	9 (15.5)	7 (2.8)
	cN0 & pN0	453 (79.6)	399 (61.8)	74 (51.7)	787 (46.6)		cN0 & pN0	75 (76.5)	73 (57.5)	26 (44.8)	120 (47.8)
Buccal Mucosa:											
	level	T1	T2	T3	T4						
n		371	593	221	398						
NODAL_DISEASE (%)	cN+ & pN+	49 (13.2)	166 (28.0)	79 (35.7)	199 (50.0)						
	cN+ & pN0	11 (3.0)	28 (4.7)	16 (7.2)	49 (12.3)						
	cN0 & pN+	28 (7.5)	98 (16.5)	25 (11.3)	27 (6.8)						
	cN0 & pN0	283 (76.3)	301 (50.8)	101 (45.7)	123 (30.9)						

Table 1 Clinical and pathologic staging information for oral cavity SCC tumors based on subsite and tumor stage (T stage). cN+: Clinically nodal positive, cN-: Clinically nodal negative, pN+: Pathologically nodal positive, pN-: pathologically nodal negative.

Results

Tumor and nodal staging for patients who underwent primary surgery and neck dissection are listed in **Table 1**. Rates of nodal metastasis varied between the primary tumor sites, but were lowest for the mucosal lip (15.4%), and highest for retromolar area (48.3%) and floor of mouth (44.2%) locations. The rate of occult nodal metastasis for T1 and T2 tumors was highest for the oral tongue (T1= 10.9%, T2= 20.7%) and retromolar area (T1= 12.4%, T2= 17.7%). This rate was lowest for tumors of the mucosal lip (T1= 2.0%, T2= 7.9%) and hard palate (T1= 2.0%, T2= 12.6%). The alveolar ridge was the most likely site to present with T4 tumor stage (55.4%). The mucosal lip and oral tongue were the most likely sites to present with lower tumor stages (T1 or T2) at 81.4% and 81.7%, respectively. Patients with clinically positive nodal disease and pathologically negative nodal disease were deemed to have false positive diagnosis of neck metastasis. This false positive rate was highest for mucosal lip tumors at 1.5%, 4.4%, 20.6%, and 13.2% for T1, T2, T3, and T4 tumors, respectively.

Elective neck dissection (END) data was collected and listed in **Table 2**. An END was performed for 46.3%, 59.9%, and 54.3% for T1, T2, and T3 tumors respectively, however these rates of elective neck dissections varied between the different oral cavity subsites. Patients with primary tumors of the oral tongue had the highest rate of END performed for early-staged cancers (49.5% for T1 and 64.5% for T2). Rates of END were lowest for patients with mucosal lip tumors (26.1% for T1, 38.8% for T2) and for the hard palate (29.2% for T1, 32.2% for T2). When an END was performed the overall rate of occult nodal disease was 11.1%, 26.3%, and 35.0% for T1, T2, and T3 tumors respectively. END was most likely to diagnosis occult nodal disease for tumors involving the oral tongue (12.3% for T1, and 30.0% for T2) and the retromolar area (15.8% for T1 and 27.8% for T2). This rate of an elective neck dissection uncovering occult nodal disease was lowest for the mucosal lip (2.0% for T1, and 9.8% for T2).

Primary Site	cN0 (n)	pN0 + pN+ (n)	Rate of elective neck dissection (%)	Floor of Mouth	cN0 (n)	pN0 + pN+ (n)	Rate of elective neck dissection (%)
All Sites				Overall	5933	3137	52.9
Overall	30248	15846	52.4	T1	2548	1180	46.3
T1	14590	6756	46.3	T2	1772	1055	59.5
T2	9259	5549	59.9	T3	341	181	53.1
T3	1937	1051	54.3	T4	1272	721	56.7
T4	4462	2490	55.8	Hard Palate			
Lip				Overall	980	328	33.5
Overall	1081	327	30.2	T1	264	77	29.2
T1	750	196	26.1	T2	276	89	32.2
T2	237	92	38.8	T3	97	35	36.1
T3	51	17	33.3	T4	343	127	37.0
T4	43	22	51.2	Buccal mucosa			
Tongue				Overall	1973	986	50.0
Overall	15062	8260	54.8	T1	724	311	43.0
T1	8690	4303	49.5	T2	698	399	57.2
T2	4912	3166	64.5	T3	230	126	54.8
T3	945	548	58.0	T4	321	150	46.7
T4	515	243	47.2	Retromolar area			
Alveolus				Overall	1503	785	52.2
Overall	3716	2023	54.4	T1	433	196	45.3
T1	1181	493	41.7	T2	517	259	50.1
T2	847	489	57.7	T3	118	55	46.6
T3	155	89	57.4	T4	435	275	63.2
T4	1533	952	62.1				

Table 2 Data on elective neck dissection. cN0: Patients with no clinical evidence of lymph node metastasis. pN0: Patients who had elective neck dissection performed and had no pathologic evidence of metastatic lymph nodes, pN+: Patients who had elective neck dissection that yielded metastatic lymph nodes

Discussion & Conclusions

The presentation and propensity for cervical metastasis in OCSCC varies based on the primary site of tumor involvement. Evaluation and treatment of these patients should take into consideration the likelihood of clinical and occult metastasis for the specific primary tumor location.

Oral Tongue- The rate of positive nodal yield in END was 14.0% and 42.8% for T1 and T2 respectively. This data corroborates previous literature that shows even small primary SCC of the oral tongue have the ability to spread. The senior author's current preference is to perform an elective neck dissection for all T1N0 SCC of the oral tongue with a DOI of >2mm.

Floor of Mouth- Given the 11.2% yield of cancerous nodes with END performed for T1 tumors, debate on how to properly manage T1N0 SCC will likely continue until more convincing evidence regarding management and outcomes is reported. However, END should be strongly recommended in patients with T2N0 FOM SCC given the 27.3% yield of cancerous nodes found in these cases.

Hard Palate, Maxillary alveolus- The yield of cancerous nodes with END for T1 tumors was 2.6%. However, this rate increased to 18.0% and 25.7% for T2 and T3 tumors respectively. Therefore, an elective neck dissection should be strongly encouraged for all hard palate and maxillary alveolar SCC tumors staged T2 and above.

Mucosal Lip- The mucosal lip had low rate of occult metastasis and low yields of elective neck dissections, and the usefulness of performing END in the setting of a T1N0 or T2N0 mucosal lip SCC appears limited.

Buccal- The yield for uncovering occult nodal disease with END was 9.0% and 24.6% for T1 and T2 tumors respectively. Based on the low rates of occult nodal metastasis for T1 tumors, this data augments the findings by Fang et al. which showed no survival benefit of elective neck dissection for T1 tumors⁵. However, taking into account higher rate of recurrence and occult nodal metastasis, no such conclusion can be made for T2N0 SCC of the buccal mucosa.

Retromolar area- Based on the high rates of END uncovering occult nodal disease (15.5% for T1 and 27.8% for T2 tumors) an elective neck dissection should be recommended for all T1N0 and T2N0 SCC of the retromolar area treated with primary surgery.

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