Differences in Predictors for Oral Tongue Squamous Cell Carcinoma Survival as Stratified by Age and Sex: A SEER Analysis

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ABSTRACT

IMPORTANCE: At the conclusion of this presentation, the participants should be able to recognize the differences in predictors of survival for oral tongue squamous cell carcinomas as stratified by age (40 years and younger vs. older than 40) and sex.

OBJECTIVE: To utilize the Surveillance, Epidemiology, and End Results (SEER) database to elucidate differences in predictors of survival in oral tongue SCC as stratified by age and sex.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective population-based analysis.

MAIN OUTCOMES AND MEASURES: The SEER registry was utilized to calculate survival trends for patients with oral tongue SCC between 1973 and 2012. Patient data was then stratified by age (<=40 years vs. >40 years) and sex, then analyzed with respect to race, stage, grade, and treatment modalities. Overall (OS) and disease-specific survival (DSS) were calculated and compared.

RESULTS: 16,423 cases of oral tongue SCC were identified, with 526 and 706 young female and male patients, respectively. Young female patients had improved OS and DSS as compared to young male patients (75% vs. 67% at 5 years), which is better than older patients (p<0.001). Younger patients were more likely to receive surgery (p <0.001) and combination surgery and radiation (p <0.001) as compared to older patients. On multivariate analysis, tumor stage was uniformly associated with worse OS and DSS (p<0.05), with surgery predicting improved OS and DSS in all groups except young females (p<0.05). Interestingly, higher tumor grade predicted worse OS and DSS in older patients, but not younger patients (p<0.05).

CONCLUSIONS AND RELEVANCE: Despite being a relatively common head and neck malignancy, oral tongue SCC appears to present with relatively heterogeneous characteristics across different age groups and sexes. Young female patients were found to have overall good prognosis. Tumor grade may play a role in prognostication in older patients.

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INTRODUCTION

Recent epidemiological studies have noted the increasing incidence of head and neck cancer among young adults, particularly tongue and oropharyngeal neoplasms.[1] The cause of this rise remains unclear; however many mechanisms have been proposed including carcinogenic exposures, genetic predisposition or viral infections.[2] In this study, we aim to compare differences in survival and prognosticators among men and women with oral tongue (OT) cancer younger than 40 years compared to those older than 40 years.

METHODS

Using the SEER database, appropriate cases were queried and selected in order to calculate summary statistics and survival trends for patients with a diagnosis of oral tongue cancer between January 1, 1973 and January 1, 2012. Site-specific codes were checked to ensure that primary sites were limited to the oral tongue; cases that did not originate within this subsite were excluded from the analysis. Patient demographic and clinical data, including histopathology, age, sex, race, primary site, treatments rendered (surgery and/or radiation), and survival (overall and disease-specific) were compiled.

Primary outcomes for the study included overall survival (OS), or time from initial treatment to death from any cause, and disease-specific survival (DSS), or time from initial treatment to death from OT SCC and malignancy-related causes. Kaplan-Meier curves based on OS and DSS were constructed and stratified by tumor stage, with differences evaluated by the log-rank test. Univariate and multivariate regression using the Cox proportional hazards model was used to evaluate covariates affecting OS and DSS. For the multivariate analysis, covariates were chosen based on significance on univariate analysis; surgical therapy as a covariate was added in context of its clinical significance. Statistical analysis was performed using SPSS 21 (IBM Corporation, Armonk, NY). A significance level of 0.05 was used for all tests.

RESULTS

A total of 526 cases of young female and 706 cases of young male OT SCC were identified out of 16,423 cases of OT SCC in the database and met inclusion criteria. The median OS of young male and female OT SCC were 248 and 468 months, respectively, while OS of OT SCC in men and women > 40 years older than were 57 and 75 months. Table 1 and 3 displays the demographic and survival data for the study population. On univariate and multivariate analysis (Tables 2 and 4), tumor stage was uniformly associated with worse OS and DSS (p<0.05), with surgery predicting improved OS and DSS in all groups except young females (p<0.05).

	All cases (n=16423)	Females ≤ 40 (n=526)	Males ≤ 40 (n=706)	Females > 40 (n=6296)	Males > 40 (n=8895)	
Age	**Years**					
Mean	61.6 ± 14.1	33.3 ± 5.6	33.4 ± 5.6	65.9 ± 12.4	62.5 ± 11.3	
Minimum	12	12	14	41	41	
Maximum	85	40	40	85	85	
	Proportion (n)					***p***
Race						
White	85.8% (13984)	82.0% (427)	81.9% (573)	85.5% (5383)	86.1% (7601)	
Black	6.2% (1004)	4.2% (22)	6.6% (46)	5.2% ((325)	6.9% (611)	<0.001
Other	8.0% (1309)	13.8% (72)	11.6% (81)	8.6% (540)	7.0% (616)	
Subsite						
Lateral	40.7% (6689)	45.6% (240)	45.3% (320)	41.3% (2600)	39.7% (3529)	
Anterior 2/3 NOS	31.0% (5094)	29.3% (154)	29.2% (206)	31.5% (1986)	30.9% (2748)	<0.001
Ventral	19.9% (3274)	16.5% (87)	17.6% (124)	18.4% (1158)	21.4% (1905)	
Dorsal	8.3% (1366)	8.6% (45)	7.9% (56)	8.8% (552)	8.0% (713)	
Treatment						
Surgery	85.1% (13814)	93.1% (487)	90.1% (631)	86.4% (5386)	83.4% (7310)	<0.001
Radiation	37.5% (6051)	39.6% (203)	43.3% (300)	34.6 (2139)	39.1% (3409)	<0.001
Both	27.1% (4342)	35.1% (181)	35.6% (251)	25.1% (1545)	27.3% (2365)	<0.001
T						
1	55.6% (3885)	61.9% (151)	49.1% (131)	59.5% (1631)	52.7% (1972)	
2	27.8% (1946)	24.6% (60)	33.3% (89)	26.9% (738)	28.3% (1059)	
3	8.8% (615)	8.6% (21)	10.5% (28)	7.1% (195)	9.9% (371)	<0.001
4	7.8% (544)	4.9% (12)	7.1% (19)	6.4% (176)	9.0% (337)	
N						
0	73.3% (5634)	71.0% (186)	67.1% (192)	75.3% (2291)	72.4% (2965)	
1	11.6% (888)	13.0% (34)	13.6% (39)	11.7% (355)	11.2% (460)	
2	14.5% (1118)	16.0% (42)	18.9% (54)	12.6% (383)	15.6% (639)	
2a	1.1% (79)	1.1% (3)	2.2% (6)	0.8% (24)	1.1% (46)	0.001
2b	10.7% (745)	11.8% (31)	14.2% (38)	8.8% (269)	9.9% (407)	
2c	3.8% (263)	2.7% (7)	3.4% (9)	2.8% (85)	4.0% (162)	
3	0.6% (47)	0	0.3% (1)	0.4% (13)	0.8% (33)	
M						
0	98.9% (7612)	99.2% (257)	100% (286)	99.1% (3020)	98.6% (4049)	0.036
1	1.1% (88)	0.8% (2)	0	0.9% (27)	1.4% (59)	
Stage						
1	48.0% (3347)	50.2% (121)	42.1% (112)	51.3% (1396)	46.0% (1718)	
2	17.0% (1184)	14.1% (34)	18.4% (49)	16.7% (454)	17.3% (647)	
3	14.0% (978)	16.6% (40)	15.8% (42)	13.6% (371)	14.0% (525)	<0.001
4	20.9% (1457)	19.1% (46)	23.7% (63)	18.4% (501)	22.7% (847)	
Grade						
Well differentiated	28.9% (4131)	27.4% (129)	28.3% (179)	30.7% (1675)	27.8% (2148)	
Moderately differentiated	54.0% (7711)	52.0% (245)	54.2% (343)	52.5% (2865)	55.1% (4258)	
Poorly differentiated	16.7% (2389)	20.2% (95)	17.1% (108)	16.3% (890)	16.8% (1296)	0.031
Undifferentiated	0.4% (55)	0.4% (2)	0.5% (3)	0.4% (22)	0.4% (28)	

Table 1. Demographics of cases compiled from the SEER registry

	All cases		Female ≤ 40		Male ≤ 40		Female > 40		Male > 40	
Characteristic	**OS**	**DSS**	**OS**	**DSS**	**OS**	**DSS**	**OS**	**DSS**	**OS**	**DSS**
Age	<0.001	<0.001	0.353	0.345	0.674	0.456	<0.001	<0.001	<0.001	0.012
Race	<0.001	<0.001	0.020	0.168	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Subsite	<0.001	<0.001	0.061	0.036	0.024	0.181	<0.001	<0.001	<0.001	<0.001
Surgery	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Radiation	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Surgery and radiation	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
T	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
N	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
M	<0.001	<0.001	<0.001	<0.001	NR	NR	<0.001	<0.001	<0.001	<0.001
Stage	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Grade	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 2. Univariate analysis of predictors of overall and disease free survival stratified by age and gender

DISCUSSION

OT SSC affecting young adults appears to be a different clinical entity than that of older adults. HPV-related oropharyngeal carcinoma is a model of the impact of epidemiological study resulting in proposed de-escalated treatment that maximizes survival but preserves function. From this analysis, it appears that OT SCC affecting young females has a better survival than OT SCC of young men and older adults. Furthermore, tumor grade may prognosticate survival in older adults but does not affect survival in younger adults. There is marked heterogeneity in OT SCC across different age groups and sexes suggesting that OT behaves differently from other types of HNSCC.

Median survival (months)	**OS**	**DSS**
All cases	74.8	361.3
Female ≤ 40	468	468
Male ≤ 40	248.8	480
Female > 40	74.8	361.3
Male > 40	57.4	281.1

	2 yr		5 yr		10 yr	
Percent survival (%)	**OS**	**DSS**	**OS**	**DSS**	**OS**	**DSS**
All cases	68.2%	79.8%	53.7%	73.2%	38.4%	66.9%
Female ≤ 40	80.2%	81.8%	74.7%	76.7%	69.4%	73.8%
Male ≤ 40	74.7%	78.6%	66.8%	71.9%	61.1%	68.1%
Female > 40	68.2%	79.8%	53.7%	73.3%	38.4%	66.9%
Male > 40	65.4%	77.9%	48.9%	69.7%	33.2%	63.1%

Table 3. Median and 2, 5, and 10-year overall and disease-specific survival stratified by age and gender

	Overall survival (OS)		Disease-specific survival (DSS)	
	HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
All cases				
Age	1.03 (1.028-1.034)	<0.001	1.02 (1.01-1.03)	<0.001
Sex	1.14 (1.05-1.24)	0.002		0.999
Race		0.903	1.10 (1.01-1.20)	0.034
Subsite	1.06 (1.02-1.10)	0.006	1.08 (1.02-1.14)	0.010
Surgery	0.37 (0.33-0.42)	<0.001	0.36 (0.31-0.41)	<0.001
Radiation	0.81 (0.73-0.89)	<0.001		0.320
Stage	1.59 (1.52-1.65)	<0.001	1.85 (1.75-1.96)	<0.001
Grade	1.39 (1.30-1.48)	<0.001	1.30 (1.19-1.43)	<0.001
Female ≤ 40				
Race		0.330		0.560
Subsite		0.725		0.805
Surgery		0.064		0.059
Radiation		0.768		0.564
Stage	1.70 (1.20-2.39)	0.003	1.84 (1.26-2.69)	0.002
Grade		0.298		0.186
Male ≤ 40				
Race		0.959		0.642
Subsite		0.339		0.070
Surgery	0.34 (0.17-0.67)	0.002	0.34 (0.17-0.68)	0.003
Radiation		0.489		0.161
Stage	1.71 (1.31-2.22)	<0.001	1.78 (1.33-2.39)	<0.001
Grade		0.285		0.814
Female > 40				
Race		0.812	1.16 (1.01-1.33)	0.034
Subsite		0.206		0.110
Surgery	0.27 (0.23-0.33)	<0.001	0.31 (0.25-0.40)	<0.001
Radiation	0.73 (0.62-0.86)	<0.001		0.825
Stage	1.55 (1.45-1.65)	<0.001	1.70 (1.55-1.87)	<0.001
Grade	1.55 (1.39-1.72)	<0.001	1.52 (1.32-1.76)	<0.001
Male > 40				
Race		0.437		0.453
Subsite		0.107		0.183
Surgery	0.38 (0.33-0.44)	<0.001	0.37 (0.31-0.45)	<0.001
Radiation	0.72 (0.63-0.82)	<0.001	0.80 (0.67-0.96)	0.017
Stage	1.55 (1.47-1.64)	<0.001	1.96 (1.80-2.12)	<0.001
Grade	1.24 (1.14-1.35)	<0.001	1.15 (1.02-1.30)	0.025

Table 4. Multivariate analysis of overall and disease specific survival stratified by demographics, treatment, and clinicopathologic data as a function of gender and age.

REFERENCES

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