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A comparative evaluation of outcomes between tongue SCC and ACC of salivary glands: retrospective match-case study

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ABSTRACT

Introduction: The aim of this study was to assess Tongue Squamous Cell Carcinoma (TSCC) patients' outcome and compare that to their matched pair counterparts of salivary gland adenoid cystic carcinoma (SGACC) patients.

Materials and Methods: A population-based cohort study was conducted using SEER data. From a database of 2019 patients, treated from 2004 to 2012. We matched individuals with tongue SCC to those who have ACC of salivary gland. Matches were made for gender, age and treatment modalities. We compared their 5-year survival, rate of local, regional and distant failures.

Results: We identified 1716 patients with TSCC and 313 cases with SGACC. Median follow up time was 2.07 years. The frequency of SGACC was significantly high in female likewise the frequency of TSCC in males ($p \leq 0.001$). SGACC tumor was more likely to be detected at an advanced stage ($p \leq 0.001$). The most often affected subsites in the TSCC tumor were the tongue (C02.9) (24.5%) and in SGACC tumor were the minor salivary gland (42.5%). There was a significant ($P \leq 0.001$) difference in overall survival in favor of female with SGACC and the combined-therapy group over the TSCC patients belong to the same group. The Kaplan–Meier estimates of overall survival at five years were 58% in the TSCC patients and 87% in the SGACC group.

Conclusion: It is important for the clinicians be aware of the invasive nature of oral malignancies especially TSCC and SGACC. These lesions are associated with high recurrence rate and distant metastasis and poor prognosis. Early detection may enhance the survival rate of the patients. The overall survival is lower in TSCC than SGACC and the death rate is higher in these kinds of tumors.

Key words: Diagnostics, Salivary glands, Cancer and pre-cancer, Squamous cell carcinoma.

Introduction

Malignancies of the oral cavity and pharynx are one of the 10 most common types of cancer in the United States [1] with an estimated 45,780 new cases and 8,650 deaths expected in 2015 [2]. Oral squamous cell carcinoma (SCC) which is the most common oral cancer, affects about 30,000 people in the U.S each year [3]. SCCs originating in the oral tongue have been demonstrated to have a worse prognosis than those arising in other subsites of oral cavity, with high risk of developing local recurrence [4, 5]. The 5-year survival rates for patients in stages III and IV are 30-50%, decreasing to 15-30% in patients with lymph node metastasis [6].

Another important neoplasm of head and neck area is adenoid cystic carcinoma (ACC) which is the third most common malignant salivary gland tumor overall [7], that because of its high tendency of distant metastasis and multiple recurrences, the management of the disease is still challenging [8,9]. The five-year survival rate for patients that has not spread at the time of diagnosis is 91%. If the

cancer has spread to the surrounding lymph nodes the five-year survival rate is 75%. If the cancer has distant metastasis the five-year survival rate is 39% [10]. The worst prognosis is related to these two types of malignancy in the maxillofacial fields. The aim of this study was to assess tongue SCC patients' outcome and compare that to their matched pair counterparts of salivary gland patients.

Material and Methods

A retrospective cohort study was conducted using information from the SEER public-use data 1973-2012 program of national cancer institute [11]. From a database of 2019 patients, treated from 2004 to 2012, we matched individuals with tongue SCC to those who have ACC of salivary gland and had the following identical prognostic factors: no distant metastasis, no cervical lymph nodes, age (older than 40 years). Matches were also made for gender and treatment modalities. Patients with "data not available" and carcinoma "in situ" were excluded from analysis. We compared their 5-year survival, rate of local, regional and distant failures. Five-year survival rates were estimating by the Kaplan-Meier method and the significant of differences among survival curves was calculated by log-rank test. Independent sample t-test and analysis were used to determine statistically significant differences between the patient characteristics. Data provided by SEER * Stat software [12] and Statistical calculations were performed using the R (free software). For all tests, significant achieved when p-value < 0.05.

Result

We identified 1716 patients with TSCC and 313 cases with SGACC who fulfilled all inclusion criteria. These patients were stratified into four groups according to sex and treatment modalities, in order to compare outcomes. Median follow up time was 2.07 years with an average of 3.12 years. The differences between TSCC and SGACC in patient and tumor characteristics are summarized in table 1.

The frequency of SGACC was significantly high in female likewise the frequency of TSCC in males (p=0.000). Both TSCC and SGACC occur relatively more frequently in the white race than in other races (p=0.025). SGACC tumor was more likely to be detected at an advanced stage (p=0.000). There are significant mean differences between tumor size (p=0.000) but there are not between age at diagnosis (p=0.933). 232 patients of SGACC (68.4%) underwent surgery with postoperative radiotherapy and107 patients (31.6%) underwent surgery alone, In comparison with TSCC patients, 381 patients of SGACC (22.2%) underwent surgery with postoperative radiotherapy and 1335 patients (77.8%) underwent surgery alone. Among TSCC patients, 40 (2.33%) recurrence tumor,26 (1.52%) distant metastasis and 49 (14.5%) death were observed, whereas among patients with SGACC, just 2 (0.61%) cases have a recurrence, 13 (4.02%) cases have distant metastasis and 441 (25.7%) cases has died. These characteristics are also illustrated by figure 1.

The most often affected subsites in the TSCC tumor were the tongue (C02.9) (24.5%) and in SGACC tumor were the minor salivary gland (42.5%) (table.2).

There was a significant (P=0.000) difference in overall survival in favor of female with SGACC and the combined-therapy group over the TSCC patients belong to the same group (fig2.1). The estimated mean time to death was 6.99 years (95% confidence interval, 6.59 to 7.38) in the SGACC patients and 5.37 years (95% confidence interval, 4.82 to 5.92) in the TSCC patients (table 3.1). The Kaplan–Meier estimates of overall survival at five years were 58% in the TSCC patients and 87% in the SGACC group. In contrast, comparison of overall survival for female with surgery alone-therapy group failed to show a significant difference (P =0.298) (fig 2.2). This comparison is done between in male groups with two different treatment modalities.

SGACC male Patients who received radiotherapy after surgery had significantly better survival than those who have TSCC (p=0.000). As illustrate in Fig 2.3. But there is no survival difference was observed between TSCC and SGACC male patients who received surgery alone (p=0.360) (fig. 2.4).

Discussion

Malignancies of head and neck area are the sixth cause of cancer death all around the word [13]. The number of patients suffering from the oral cancers are increased in various populations during past decades [14]. Early diagnosis and treatment of oral malignancies as a part of head and neck area are the important factors in improving the survival rate of patients. Squamous cell carcinoma (SCC) is responsible for 95% of oral cavity malignancies [15]. Adenoid cystic carcinoma (ACC) is another serious malignancy of oral cavity which account for 2 to 4% of all head and neck cancers [16]. Current study aimed to present the long term out-

comes of patients with SCC of the tongue compared to the salivary gland patients with ACC using SEER database.

The incidence of TSCC was significantly higher in white races and females. Female to male ratio was 2 to 1 which was similar to some other researches [17], although this ratio was either lower [18] or slightly higher [15] in some other reports. The five year survival rate of TSCC patients was relatively higher than other similar investigations [15, 18]. Bell et al. (2007) reported similar survival rate to current study [19]. They evaluated the survival rate of different subsites of oral SCC. The recurrence and metastasis of tongue SCC in Bell's study was higher than current survey (13.6% versus 2.32% and 6% versus 1.52% respectively).

ACC of salivary glands is the second most common malignancy of salivary tumors which is characterized by poor prognosis among the salivary gland neoplasms [20]. Rapidis et al. (2004) reported the cinicopathological features of ACC of 23 patients [21]. Local recurrence was observed in 23% of the cases. The mean survival of the patients was 70.58 months. They represented high incidence of distant metastasis which occurred in 47.8% of the cases. Triantafillidou et al. (2006) represented the management of ACC of 22 patients. The local recurrence and distant metastasis was significantly less than the measures presented in Rapidis et al. study (9% respectively for both occurrence) [16]. The overall mean survival of the patients in our study was 83.88 months. Local recurrence and distant metastasis were occurred in 0.61 and 4.02% of the patients respectively.

The treatment of oral malignancies especially SCC and ACC is puzzling due to the possibility of local recurrence, distant metastasis and aggressive nature [16]. The treatment plan for SCC and ACC is multidisciplinary which is consisted of surgical removal and radiotherapy [16, 22]. The treatment plan of SCC is affected by several factors including age, tumor size, stage, grade, distant metastasis, and perineural invasion [19]. Fordice et al. (1999) analyzed the treatment plans of ACC patients. Their study yielded that combined treatment consisted of surgery and postoperative radiotherapy was satisfactory [23]. Maciejewskiet al. (2002) reported the outcomes of surgery on ACC patients. They yielded that there is a high risk of local recurrence after surgical resection of the tumor. They suggested that postoperative radiation therapy is essential following surgical removal of ACC [24]. In current study radiotherapy was administered in 68.4% of ACC patients who went under surgical procedure. The overall survival was significantly higher in the male patients who underwent combined therapy.

Combined therapy is essential in treatment of oral SCC. Surgical resection of the lesion is primary treatment procedure which should be followed by radiotherapy and chemotherapy. It becomes more clear by considering the poor prognosis of TSCC compared to SCC of other oral areas [15, 25]. Surgical procedure was performed on 77.8% of TSCC patients alone. The overall survival was not affected by administering radiation therapy or not. These findings are related to the surgical procedure. Actually the ability to remove the SCC lesion totally with free margins is important in enhancing the survival rate of the patients. The ability to treat the patients very well is regarded to the stage of the disease. In fact the stage of TSCC is an important predictor factor in estimating the survival rate of the patient.

Findings of current study indicate that local recurrence of TSCC is higher than SGACC although distant metastasis occurs predominantly in SGACC patients. The patients suffered from SGACC were treated more by combined therapy and overall survival in favor of female patients with SGACC and the combined-therapy group over the TSCC patients belong to the same group was significantly higher. The same findings were significant in male patients; however these findings were not significantly different in surgery alone groups. The five year survival rate was significantly higher in SGACC patients than TSCC ones.

Choosing the appropriate and effective modality is affected by various factors. Stage of the tumors is an important point should be considered before choosing the right treatment plan. According to the findings of current survey patients with SGACC were likely more in the advanced stages; however more TSCC lesions were in T1 stage. These findings influenced on the selection of the appropriate modality. So the patients with SGACC were treated more by combined therapy than TSCC patients.

Conclusion

It is important for the clinicians be aware of the invasive nature of oral malignancies especially SCC and ACC. These lesions are associated with high recurrence rate and distant metastasis and poor prognosis. Early detection may enhance the survival rate of the patients. The overall survival is lower in TSCC than SGACC

and the death rate is higher in these kinds of tumors.

Table 1: Patient and Tumor characteristics.

Patients Characteristic		*Primary Site*		*P-value*
		Salivary Gland	*Tongue*	*x^2_test*
Sex	*Female*	*198 (58.4%)*	*667 (38.9%)*	*0.000*
	Male	*141 (41.6%)*	*1049 (61.1%)*	
Race	*White*	*268 (79.1%)*	*1455 (84.8%)*	*0.025*
	Black	*24 (7.1%)*	*78 (4.5%)*	
	*Other**	*47 (13.9%)*	*183 (10.7%)*	
T-Stage	*T1*	*128 (37.8%)*	*1041 (60.7%)*	*0.000*
	T2	*104 (30.7%)*	*497 (29.0%)*	
	T3	*55 (16.2%)*	*114 (6.6%)*	
	T4a	*41 (20.2%)*	*61 (3.6%)*	
	T4b	*11 (3.2%)*	*3 (0.2%)*	
Treatment modalities	*Surgery alone*	*107 (31.6%)*	*1335 (77.8%)*	
	Radiation after surgery	*232 (68.4%)*	*381 (22.2%)*	
Treatment failure	*Recurrence*	*2 (0.61%)*	*40 (2.33%)*	*0.002*
	Metastases	*13 (4.02%)*	*26 (1.52%)*	
Vital Status	*Alive*	*290 (85.5%)*	*1275 (74.3%)*	*0.000*
	Dead	*49 (14.5%)*	*441 (25.7%)*	
				t-test
Tumor size	*Mean (mm)*	*34.87*	*58.90*	*0.000*
Age at diagnosis	*Mean (year)*	*62.19*	*62.26*	*0.933*

Table 2: Frequency of subsite's tumor

Subsite (Tongue)	*Frequency (%)*	*Subsite (Salivary Gland)*	*Frequency (%)*
(C01.9) Base of tongue	*323(18.8%)*	*(C07.9) Parotid gland*	*80(23.6%)*
(C02.0) Dorsal surface of tongue	*54(3.1%)*	*(C08.0) Submandibular gland*	*97(28.6%)*
(C02.1) Border of tongue	*349(20.3%)*	*(C08.1) Sublingual gland*	*10(2.9%)*
(C02.2) Ventral surface of tongue	*244(14.2%)*	*(C08.9) Major Salivary gland*	*8(2.4%)*
(C02.3) Anterior 23| of tongue	*327(19.1%)*	*Minor Salivary gland*	*118(42.5%)*
(C02.9) Tongue	*419(24.5%)*	-	-
Total	*1716 (100%)*		*313(100%)*

Table 3.1: Mean survival in patients with M0_N0_Tany_Female_older than 40_Surgery+RT.

Primary Site	Mean			
	Estimate	95% Confidence Interval		
		Std Error	Lower Bound	Upper Bound
Salivary Gland	6.990	0.200	6.599	7.382
Tongue	5.372	0.281	4.822	5.922
Overall	6.155	0.181	5.800	6.511

Log Rank Test=18.511 p=0.000.

Table 3.2: Mean survival in patients with M0_N0_Tany_Female_older than 40_noRT.

Primary Site	Mean			
	Estimate	95% Confidence Interval		
		Std Error	Lower Bound	Upper Bound
Salivary Gland	6.90	0.363	6.197	7.620
Tongue	6.33	0.131	6.084	6.596
Overall	6.38	0.123	6.149	6.631

Log Rank Test=1.089 p=0.298.

Table 3.3: Mean survival in patients with M0_N0_Tany_Male_older than 40_Surgery+RT.

Primary Site	Mean			
	Estimate	95% Confidence Interval		
		Std Error	Lower Bound	Upper Bound
Salivary Gland	7.362	.214	6.943	7.782
Tongue	5.298	.166	4.973	5.624
Overall	5.651	.147	5.362	5.940

Log Rank Test=27.343 p=0.000.

Table 3.4: Mean Survival in patients with M0_N0_Tany_Male_ older than 40_noRT.

Primary Site	Mean			
	Estimate	95% Confidence Interval		
		Std Error	Lower Bound	Upper Bound
Salivary Gland	6.227	0.501	5.244	7.209
Tongue	6.511	0.166	6.186	6.837
Overall	6.478	0.158	6.169	6.788

Log Rank Test=0.838 p=0.360

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA: a cancer journal for clinicians. 2013;63(1):11-30.

[2]] Bethesda M. SEER Cancer Statistics Factsheets: Oral Cavity and Pharynx Cancer. http://seer.cancer.gov/statfacts/html/oralcav.html: National Cancer Institute; [10-may-2015].

[3] Bradley S. Oral Squamous Cell Carcinoma. http://www.merckmanuals.com/professional/ear-nose-and-throat-disorders/tumors-of-the-head-and-neck/oral-squamous-cell-carcinoma: Merck; [10-may-2015].

[4] Rusthoven KE, Raben D, Song JI, Kane M, Altoos TA, Chen C. Survival and patterns of relapse in patients with oral tongue cancer. Journal of Oral and Maxillofacial Surgery. 2010;68(3):584-9.

[5] McDowell L, Collins M, Kleid S, Rischin D, Corry J. T4 squamous cell carcinoma of the oral tongue without mandibular involvement: surgery or chemoradiotherapy? Oral surgery, oral medicine, oral pathology and oral radiology. 2014;117(2):163-9.

[6] Gosselin E. Malignant Tumors of the Mobile Tongue author. Medscape. June 2011.

[7] Fordice, Jim; Kershaw, Corey; El-Naggar, Adel; Goepfert, Helmuth (February 1999). "Adenoid Cystic Carcinoma of the Head and Neck: Predictors of Morbidity and Mortality". Archives of Otolaryngology--Head & Neck Surgery 125 (2): 149–52

[8] Ciccolallo L, Licitra L, Cantú G, Gatta G, Group EW. Survival from salivary glands adenoid cystic carcinoma in European populations. Oral oncology. 2009;45(8):669-74

[9] Shen C, Xu T, Huang C, Hu C, He S. Treatment outcomes and prognostic features in adenoid cystic carcinoma originated from the head and neck. Oral oncology. 2012; 48(5):445-9.

[10] Editor Board. Salivary Gland Cancer: Statistics. www.cancer.net: American Society of Clinical Oncology 2005-2015 [10-may-2015].

[11] Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2014 Sub (1973-2012) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S. 1969-2013 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2015, based on the November 2014 submission.

[12] Surveillance Research Program, National Cancer Institute SEER * Stat software (seer.cancer.gov/seerstat) version 8.2.1.

[13] Polanska H, Raudenska M, Gumulec J, Sztalmachova M, Adam V, Kizek R, et al. Clinical significance of head and neck squamous cell cancer biomarkers. Oral oncology. 2014;50(3):168-

[14] Sciubba JJ. Oral cancer. The importance of ear-

ly diagnosis and treatment. American journal of clinical dermatology. 2001; 2(4):239-51.

[15] Pontes FS, Carneiro JT, Jr. Fonseca FP, da Silva TS, Pontes HA, Pinto Ddos S, Jr. Squamous cell carcinoma of the tongue and floor of the mouth: analysis of survival rate and independent prognostic factors in the Amazon region. The Journal of craniofacial surgery. 2011;22(3):925-30.

[16] Triantafillidou K, Dimitrakopoulos J, Iordanidis F, Koufogiannis D. Management of adenoid cystic carcinoma of minor salivary glands. Journal of oral and maxillofacial surgery. 2006;64(7):1114-2

[17] Silverman S, Jr. Gorsky M. Epidemiologic and demographic update in oral cancer: California and national data--1973 to 1985. Journal of the American Dental Association (1939). 1990;120(5):495-9.

[18] Gorsky M, Epstein JB, Oakley C, Le ND, Hay J, Stevenson-Moore P. Carcinoma of the tongue: a case series analysis of clinical presentation, risk factors, staging, and outcome. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 2004; 98(5):546-52.

[19] Bell RB, Kademani D, Homer L, Dierks EJ, Potter BE. Tongue cancer: Is there a difference in survival compared with other subsites in the oral cavity? Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2007; 65(2):229-36.

[20] Ramsden D, Sheridan BF, Newton NC, De Wilde FW. Adenoid cystic carcinoma of the head and neck: a report of 30 cases. The Australian and New Zealand journal of surgery. 1973;43(2):102-8

[21] Rapidis AD, Givalos N, Gakiopoulou H, Faratzis G, Stavrianos SD, Vilos GA, et al. Adenoid cystic carcinoma of the head and neck. Clinicopathological analysis of 23 patients and review of the literature. Oral oncology. 2005;41(3):328-35.

[22] Akhlaghi F, Esmaeelinejad M, Shams A, Augend A. Evaluation of neo-adjuvant, concurrent and adjuvant chemotherapy in the treatment of head and neck squamous cell carcinoma: a meta-analysis. Journal of dentistry (Tehran, Iran). 2014;11(3):290-301.

[23] Fordice J, Kershaw C, El-Naggar A, Goepfert H. Adenoid cystic carcinoma of the head and neck: predictors of morbidity and mortality. Archives of otolaryngology--head & neck surgery. 1999;125(2):149-52.

[24] Maciejewski A, Szymczyk C, Wierzgon J. Outcome of surgery for adenoid cystic carcinoma of head and neck region. Journal of cranio-maxillo-facial surgery : official publication of the European Association for Cranio-Maxillo-Facial Surgery. 2002;30(1):59-61.

[25] Zelefsky MJ, Harrison LB, Fass DE, Armstrong J, Spiro RH, Shah JP, et al. Postoperative radiotherapy for oral cavity cancers: impact of anatomic subsite on treatment outcome. Head & neck. 1990;12(6):470-5.

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