HPV Associated Oral Cancer in South Texas

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Background

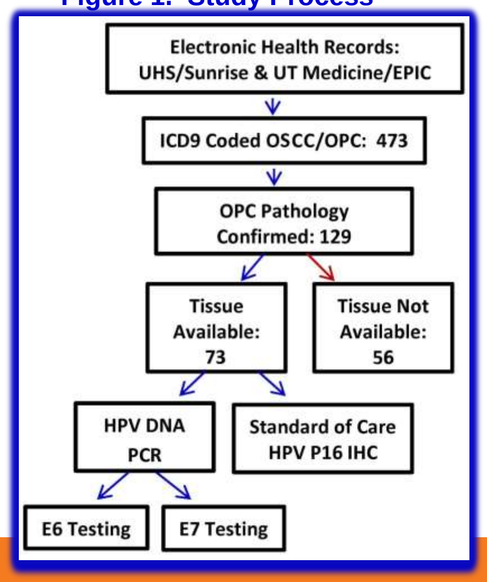
Oral human papillomavirus (HPV) infection is the fastest growing causative factor of oropharyngeal squamous cell carcinoma (OPC). HPV+ OPC accounts for 5.2% of the worldwide cancer burden and is anticipated to surpass cervical cancer incidence by 2020. HPV induces carcinogenesis by encoding two proteins, E6 and E7. E6 confers a 50 fold risk increase of developing HPV+ OPC. It will be critical to identify patients with HPV+ OPC as a group separate from other oral cancer patients.

The objective of this study was to assess the prevalence of oropharyngeal cancer among all oral cancers and thus the potential role of human papillomavirus (HPV) in this disease in the South Texas Region, from the U.S.–Mexico border, North to Williamson County, West to Eagle Pass, and East to Gonzales County, served by the University of Texas Health Science Center, San Antonio (UT Medicine) and University Health System (UHS) in San Antonio, Texas.

Materials and Methods

This retrospective cross-sectional study extracted data from electronic health records (EHR) utilizing coding data within UT Medicine and UHS systems. Data collected encompassed every patient diagnosed with oral and/or oropharyngeal cancer from 1 January 2008 through 1 July 2013. Utilizing *ICD-9* codes, 473 patients were identified. All data collected from selected databases were imported into Excel 2010 and processed to eliminate duplicate patients, diagnoses and service payment providers. Patient listings with multiple diagnosis codes for same anatomical site within 9 months of initial date of diagnosis, multiple EMR numbers or insurance methods were also removed. Validation of the data was accomplished with a random 20% comparison with UTHSCSA Head and Neck Tumor Board weekly review. Pathology reports were available in either EHR system for 129 OPC patients. Of those, formalin-fixed and paraffin-embedded (FFPE) blocks were collected from a total 73 OPC cases. 5 unstained slides were cut from each block, 2 were tested and reviewed with standard of care HPV p16 immunohistochemistry staining. Real-time quantitative polymerase chain reaction (PCR) was used to detect HPV-16 E6 and E7 DNA in the remaining 3 slides.

Figure 1. Study Process



Results

- 129 patients met inclusion criteria with an initial diagnosis of oropharyngeal cancer. The distribution of *ICD-9* codes for this subset, show the location of tumors identified, with the majority found in the base of tongue (31%), tonsils (29%) and oropharynx, NOS (23%).
- Insurance billed for the care of the *ICD-9* codes listed resulted in 35% of the population with full coverage or Medicare, 46% with limited coverage via Medicaid or county of residence, and 19% identified with indigent-out-of-county care, self-pay, or had no insurance information available.
- Of the 73 OPC patients with tissue available for testing, HPV status of subjects did not differ by age or sex (Figure 2). Our sample of females and blacks was too small to evaluate further. Among Non-Hispanics there was a two-fold higher (68.8%) positive HPV-P16 prevalence rate compared to Hispanics (31.3%), which approaches significance (*p=0.06)*.
- White Male Non-Hispanics were 3.5 times more likely to have positive HPV-P16 status compared to White Male Hispanics (Figure 3). This relationship is marginally significant (*p=0.06*) but is meaningful because it mirrors current national trend of an increasing prevalence in middle aged white males.
- There was 100% agreement between E6 and E7 PCR assays (Figure 4). There were good agreement between the two methods DNA E6 assays which closely matched the HPV P16 IHC testing (Figure 5).

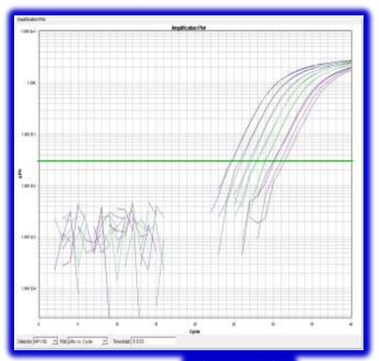
Figure 2. HPV OPC Patients Demographic Characteristics

Characteristic	HPV-P16 testing *Positive* n=32	HPV-P16 testing Negative n=41	All Subjects N=73	P-value
Age (years)				0.52
Mean (SD)	58.3 (8.8)	59.5 (9.1)	59 (8.9)	*(Mann-Whitney Test)*
Range	40,79	35,78	35,79	
Sex, n (%)				0.56
Female	5 (15.6)	9 (22)	14 (19.2)	*.(Fisher Exact Test)*
Male	27 (84.4)	32 (78)	59 (80.8)	
Race, n (%)				1
Black	0 (0)	1 (2.4)	1 (1.4)	*(Fisher Exact Test)*
White	32 (100)	40 (97.6)	72 (98.6)	
Ethnicity, n (%)				0.06*
Non-Hispanic	22 (68.8)	19 (46.3)	41 (56.2)	*(Fisher Exact Test)*
Hispanic	10 (31.3)	22 (53.7)	32 (43.8)	
Race Gender Ethnicity, n (%)				0.2
White Male Hispanic	6 (18.8)	15 (36.6)	21 (28.8)	(Fisher Exact Test)
White Male Non-Hispanic	21 (65.6)	17 (41.5)	38 (52.1)	
White Female Hispanic	4 (12.5)	7 (17.1)	11 (15.1)	
White Female Non-Hispanic	1 (3.1)	1 (2.4)	2 (2.7)	
Black Female Non-Hispanic	0 (0)	1 (2.4)	1 (1.4)	

Figure 3. Oral Cancer HPV P16 Status – Male Patients

Characteristic	Positive N=27	Negative N=32	All White Males N=59	P-value *(Fisher Exact Test)*
HPV-P16 testing n (%)				0.06*
Hispanic	6 (22.2)	15 (46.9)	21 (35.6)	
Non-Hispanic	21 (77.8)	17 (53.1)	38 (64.4)	

Figure 4. Sensitivity of HPV-16 E6 and E7 PCR



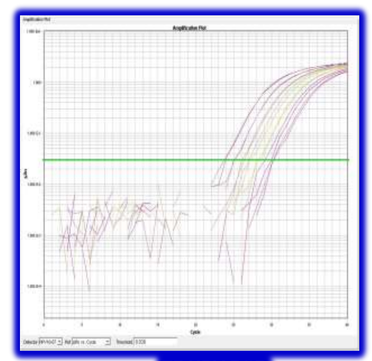


Figure 5 . HPV E6 PCR agreement to P16 IHC

	HPV-P16 IHC testing *Positive* n=32	HPV-P16 IHC testing Negative n=41	All Subjects N=73
DNA E6 PCR, n (%)			
Positive	29 (90.6)	0 (0)	29 (39.7)
Negative	3 (9.4)	41 (100)	44 (60.3)

Conclusions

Our study demonstrated that 12% of the oral cancers developed by South Texans are HPV associated oropharyngeal cancers. National data suggests that HPV associated OPC will increase over time.

Community health care providers need to recognize the change in epidemiologic factors of Human Papilloma virus associated oropharyngeal squamous cell carcinoma. Our findings support the current literature that HPV infections occur at the highest rates in white, non-Hispanic males. Accurately defining the role of HPV associated OPC in South Texas will enhance early detection and referral to definitive treatment.

Additionally, as site feasibility study, we were able to gather OPC data using electronic health record billing coding data. Unfortunately, no billing code exists in either ICD-9 or 10 for oropharyngeal HPV testing - only cervical HPV tests. Our recommendation is that, as this epidemic continues, future editions include this important link.

Source of Support: UTHSCSA Cancer Therapy and Research Center (CTRC) CPPS Pilot Award