Abstract

Human papilloma virus (HPV) is associated with increased incidence and improved prognosis in oropharyngeal cancers. Patients are typically younger and never smokers. A disproportionate number of oral tongue cancers has also been reported to arise in young non-smokers; however, the association between oral cavity squamous cell carcinoma (OCSCC) and HPV has not been established, with HPV positivity rates reported to range from 2.5% to 15.0. This is a statistically significant difference in age (p=0.041). 27 (43.5%) of the HPV-negative patients were smokers, with an average of 10.0 cumulative pack-year smoking history, as compared to 7 (33.8%) of HPV-positive patients, which was a non-significant difference (p=0.353). Alcohol use was reported by 25 (40.3%) of HPV-negative patients and 9 (69.2%) of HPV-positive subjects.

Our findings suggest that the rate of HPV-positive OCSCC may be higher than commonly reported. Similar to OP cancers, patients tend to be younger. These patients tend to have similar profiles to patients with HPV-related cancers and its with regard to smoking/alcohol status. Oral cancers should be tested for p16, and further investigation should be directed at the impact of HPV positivity on further outcomes.

Introduction

Oral cavity malignancies are widely prevalent, estimated to represent 3% of all new cancers diagnosed in 2016. Tobacco and alcohol use are well demonstrated to be associated with development of these cancers, but as use of these substances has decreased, the rate of malignancy has not decreased as would be expected. HPV (particularly high-risk subtypes HPV-16 and 18) has been well documented to be associated with the development and improved prognosis of squamous cell carcinoma in the oropharynx, but a similar relationship has not been demonstrated in malignancies of the oral cavity. Although limited by small sample size, the results did demonstrate significant difference in age of HPV positive patients (p=0.041). The average tumor size (largest dimension) was 2.58 +/- 1.78cm for HPV-positive patients and 3.34 +/- 1.81cm for HPV-negative subjects. This difference trended toward significance (p=0.087).

Patients selected for inclusion were identified by reviewing all pathology speciﬁum evaluated by the Head and Neck Pathology department between 2008 and 2012. Patients who met inclusion criteria were those who had a biopsy and/or surgical specimen diagnostic of squamous cell carcinoma of the oral cavity collected within the speciﬁed time frame. A pathology specimen was excluded if no HPV or p16 testing was performed. A retrospective chart review was then performed. Collected data included age at diagnosis, alcohol/tobacco history, ethnicity, tumor characteristics (T, N, and M stage, tumor grade, perineural invasion (PNI), lymphovascular invasion, and depth of invasion for oral tongue lesions), and treatment modality pursued. Survival and quality of life data were also collected, but was limited due to lack of long-term follow-up in this tertiary care center.

Fisher-exact tests were used to assess significance of variation between HPV-positive and HPV-negative tumors with respect to regional lymphatic spread, perineural invasion, extracapsular spread, and lymphovascular invasion. A one-tailed t-test assuming non-equal variance was used to assess significance of variance between age, T-stage, overall tumor size, and tumor grade in the two groups.

Methods and Materials

Human papilloma virus (HPV) is associated with increased incidence and improved prognosis in oropharyngeal cancers. Patients are typically younger and never smokers. A disproportionate number of oral tongue cancers has also been reported to arise in young non-smokers; however, the association between oral cavity squamous cell carcinoma (OCSCC) and HPV has not been established, with HPV positivity rates reported to range from 2.5% to 15.0. This is a statistically significant difference in age (p=0.041). 27 (43.5%) of the HPV-negative patients were smokers, with an average of 10.0 cumulative pack-year smoking history, as compared to 7 (33.8%) of HPV-positive patients, which was a non-significant difference (p=0.353). Alcohol use was reported by 25 (40.3%) of HPV-negative patients and 9 (69.2%) of HPV-positive subjects.

Our findings suggest that the rate of HPV-positive OCSCC may be higher than commonly reported. Similar to OP cancers, patients tend to be younger. These patients tend to have similar profiles to patients with HPV-related cancers and its with regard to smoking/alcohol status. Oral cancers should be tested for p16, and further investigation should be directed at the impact of HPV positivity on further outcomes.

Discussion

The rate of HPV-positive OCSCC may be higher than previously reported. These tumors tend to arise in younger patients, and may have distinct tumor characteristics. Oral cancers should be tested for HPV/p16, and further investigation should be directed at the impact of HPV positivity on patient outcomes including survival and patient quality of life.