

Effects of smoking and drinking on oropharyngeal cancer outcome by HPV serostatus

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Background

The incidence of human papillomavirus (HPV)-driven oropharyngeal cancer (OPC) continues to increase in the US. Patients with HPV-positive [HPV(+)] OPC often have a better outcome than those with HPV-negative [HPV(-)] head and neck cancer. To reduce morbidity in HPV(+) OPC, “de-escalation” strategies are being evaluated. We investigated the relationship between smoking and alcohol history at diagnosis and OPC prognosis to explore whether this easy to obtain information can aid selection of patients that can be successfully treated with less intensive therapies.

Methods

The study population consisted of 371 patients diagnosed with OPC at UPMC otolaryngology clinics [243 HPV(+), 128 HPV(-)]. Information on smoking and alcohol use were collected via questionnaires; clinical and outcome information was abstracted from medical records. HPV positivity was defined as seropositivity for antibodies against HPV16 E6 or against 3 out of 4 HPV18 E1, E2, E6, and E7 antigens. The Kaplan-Meier method and Cox proportional hazards models were used to assess the effects of smoking and alcohol use on overall survival (OS), both overall and stratified by HPV serostatus.

Results

Compared to HPV(-) patients, HPV(+) patients were significantly younger ($p=0.005$), more often male ($p<0.0001$), more often never smokers ($p=0.0008$), and smoked fewer pack-years ($p<0.0001$); no significant difference was observed in number of drinks per day or drinking status. In univariate Cox regression models, increasing drinking intensity was associated with reduced survival [HPV(+) $p=0.026$, HPV(-) $p=0.011$], but increasing pack-years smoked was not significantly associated with survival [HPV(+) $p=0.069$, HPV(-) $p=0.076$]. Controlling for age, sex, and stage, the effect of drinking intensity was retained [HPV(+) $p=0.011$, HPV(-) $p=0.015$], while the effect of pack-years smoked remained nonsignificant [HPV(+) $p=0.188$, HPV(-) $p=0.718$]. Grouping by a smoking cutoff value of two pack-years and controlling for age, sex, and stage, those with low smoking exposure had better survival than those with high exposure for both HPV-stratified groups [HPV(+) $p=0.020$, HPV(-) $p=0.023$]. In contrast, the clinically-used 10 pack-years cutoff was not associated with survival after controlling for age, sex, and stage [HPV(+) $p=0.155$, HPV(-) $p=0.092$]. In addition, a drinking intensity cutoff at one drink/day was not associated with survival after controlling for age, sex, and stage [HPV(+) $p=0.418$, HPV(-) $p=0.061$].

Conclusion

These results suggest that pack-years smoked and drinking intensity are associated with survival in both HPV(+) and HPV(-) head and neck cancer patients. A two pack-years cutoff value may be more appropriate and clinically implementable for representing pack-years smoked, while a continuous representation may be more appropriate for drinking intensity.