Human papillomavirus (HPV) has been implicated in multiple cancers, but its significance in lung cancer has remained controversial. Since the prevalence of HPV 16/18 infection was higher in lung adenocarcinoma among Taiwanese females, the aim of this study was to evaluate the clinical impact of HPV infections in lung adenocarcinoma.

Materials and Methods

Two hundred and ten patients were enrolled to investigate the associations of HPV status in tumors with clinical characteristics as well as its impact on overall survival. The methods to assess HPV status were by immunohistochemistry for HPV L1 capsid protein and E6 protein (Fig 1) and by nested polymerase chain reaction for HPV 16 and HPV 18 (Suppl Fig1).

We used Chi-square test, Kaplan-Meier estimates and Cox proportional models for statistical analyses.

Results

HPV infections were identified in 35.2% of patients, and associated with localized and smaller-sized tumors (p=0.022 and p=0.002, respectively, Table 1). Patients with HPV infections had a significantly better survival (p=0.023, by log-rank test, Fig 2) and a significantly reduced mortality risk after adjustments of age, tumor extent, epidermal growth factor receptor (EGFR) mutations status and treatments (adjusted hazard ratio [HR]=0.68, 95% confidence interval [CI]=0.49-0.96, p=0.026, by multivariate Cox proportional hazards models, Table 2). Specifically, patients with both HPV infections and EGFR mutations had the best survival outcome (one-year survival rate, 68.5% [95% CI=52.2%-84.8%]).

Conclusions

Our findings indicate that HPV infections represent an independent prognostic factor for overall survival in patients with lung adenocarcinoma. This subgroup might be preventable by HPV vaccinations.

Keywords

human papillomavirus, lung adenocarcinoma, survival