

## The Role of HPV Status in Patients with Overlapping Grey Zone Cancer in Oral Cavity and Oropharynx

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**Abstract :** Objectives: We aimed to explore the clinicodemographic characteristics and prognosis of grey zone squamous cell cancer (GZSCC) located in the overlapping or ambiguous area of the oral cavity and oropharynx and to identify valuable factors that would improve its differential diagnosis and prognosis. Methods: Information of GZSCC patients in the Surveillance, Epidemiology, and End Results (SEER) database was compared to patients with an oral cavity (OCSCC) and oropharyngeal (OPSCC) squamous cell carcinomas with corresponding HPV status, respectively. Kaplan-Meier method with log-rank test and multivariate Cox regression analysis were applied to assess associations between clinical characteristics and overall survival (OS). A predictive model integrating age, gender, marital status, HPV status, and staging variables was conducted to classify GZSCC patients into three risk groups and verified internally by 10-fold cross validation. Results: A total of 3318 GZSCC, 10792 OPSCC, and 6656 OCSCC patients were identified. HPV-positive GZSCC patients had the best 5-year OS as HPV-positive OPSCC (81% vs. 82%). However, the 5-year OS of HPV-negative/unknown GZSCC (43%/42%) was the worst among all groups, indicating that HPV status and the overlapping nature of tumors were valuable prognostic predictors in GZSCC patients. Compared with the strategy of dividing GZSCC into two groups by HPV status, the predictive model integrating more variables could additionally identify a unique high-risk GZSCC group with the lowest OS rate. Conclusions: GZSCC patients had distinct clinical characteristics and prognoses compared with OPSCC and OCSCC; integrating HPV status and other clinical factors could help distinguish GZSCC and predict their prognosis.

**Keywords :** GZSCC, OCSCC, OPSCC, HPV

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