

Interplay of Tumor Grade and HPV Status on Survival Outcomes in Sinonasal Squamous Cell Carcinoma

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Abstract

Background:

Sinonasal squamous cell carcinoma (SCC) is a rare and understudied malignancy of the head and neck. Tumor grade and human papillomavirus (HPV) status are known prognostic factors. HPV has typically portended an improved survival, while poorly differentiated tumors have shown worse survival in some cohorts. However, their combined effect on survival outcomes has not been previously evaluated.

Objective:

To investigate the combined impact of tumor grade and HPV status on overall survival in patients with sinonasal SCC using a large national database.

Study Design:

Retrospective cohort study.

Methods:

The National Cancer Database (NCDB) was queried for patients diagnosed with sinonasal SCC between 2004 and 2017. Patients with available data on tumor grade and HPV status were included. Clinicopathological features and treatment modalities were recorded. Patients were stratified into four groups based on tumor differentiation and HPV status:

- **Group 1:** Well/moderately differentiated, HPV-negative
- **Group 2:** Well/moderately differentiated, HPV-positive
- **Group 3:** Poorly differentiated, HPV-negative
- **Group 4:** Poorly differentiated, HPV-positive

Survival outcomes were assessed using Kaplan-Meier analysis and multivariable Cox proportional hazards models.

Results:

A total of 3,393 patients met inclusion criteria (mean age: 63.9 ± 13.3 years). HPV positivity was observed in 177 patients (5.2%), and 1,302 tumors (38.4%) were poorly differentiated. Multivariable analysis showed a significant interaction between tumor grade and HPV status on overall survival (Type III $p = 0.015$). Compared to Group 1, patients in Group 3 had significantly worse survival (HR = 1.13, 95% CI: 1.03–1.24, $p = 0.014$). No significant survival differences were found between Groups 2 and 4 (HR = 0.69, 95% CI: 0.43–1.10, $p = 0.118$), or between Groups 3 and 4 (HR = 1.09, 95% CI: 0.80–1.48, $p = 0.576$).

Conclusions:

Sinonasal SCC is a complex, multifaceted disease with a myriad of factors impacting the disease course. The combined influence of HPV status and tumor grade significantly impacts overall survival in sinonasal SCC, indicating these variables may interact to affect prognosis. These findings highlight that continued research into the disease biology and a thoughtful approach is warranted.

Introduction

- Sinonasal SCC is rare and poorly characterized.
- Tumor grade and HPV status are independent prognostic factors.¹⁻⁷
- Their combined effect on survival is unknown.

Table 1: Multivariate Cox Proportional Hazards Models for Overall Survival

	Hazard Ratio ^b	95% CI	P-value	Type 3 p-value
HPV/Tumor Group 1 vs 2 ^a	1.40	0.98, 2.01	0.067	0.015
HPV/Tumor Group 2 vs 1	0.71	0.50, 1.02		
HPV/Tumor Group 1 vs 3	0.89	0.81, 0.98	0.014	
HPV/Tumor Group 3 vs 1	1.13	1.03, 1.24		
HPV/Tumor Group 1 vs 4	0.97	0.71, 1.31	0.835	
HPV/Tumor Group 4 vs 1	1.03	0.76, 1.40		
HPV/Tumor Group 2 vs 3	0.63	0.44, 0.91	0.014	
HPV/Tumor Group 3 vs 2	1.58	1.10, 2.28		
HPV/Tumor Group 2 vs 4	0.69	0.43, 1.10	0.118	
HPV/Tumor Group 4 vs 2	1.45	0.91, 2.30		
HPV/Tumor Group 3 vs 4	1.09	0.80, 1.48	0.576	
HPV/Tumor Group 4 vs 3	0.92	0.67, 1.25		

^a 1: HPV- and Well/Moderately Differentiated, 2: HPV+ and Well/Moderately Differentiated, 3: HPV- and Poorly Differentiated, 4: HPV+ and Poorly Differentiated

^b Adjusted for age, race, Charlson-Deyo Score, clinical TNM stage, treatment, insurance, margins

Methods

- NCDB query of patients with sinonasal SCC between 2004 and 2017 (Figure 1).
- Patients with known tumor grade and HPV status were included.
- Survival outcomes were assessed using Kaplan-Meier analysis and multivariable Cox proportional hazards models.

Results

- Compared with HPV- well/moderately differentiated tumors, patients with HPV- poorly differentiated tumors had significantly worse survival (HR=1.13, 95% CI 1.03–1.24, $p=0.014$).
- HPV+ well/moderately differentiated nor HPV+ poorly differentiated tumors differed significantly from Group 1 after adjustment. The overall effect of HPV/tumor grade remained significant (Type 3 $p=0.015$), suggesting that the combination of HPV status and tumor differentiation independently influences survival beyond other clinical and demographic predictors.

Figure 1. Selection criteria for NCDB sinonasal SCC cohort

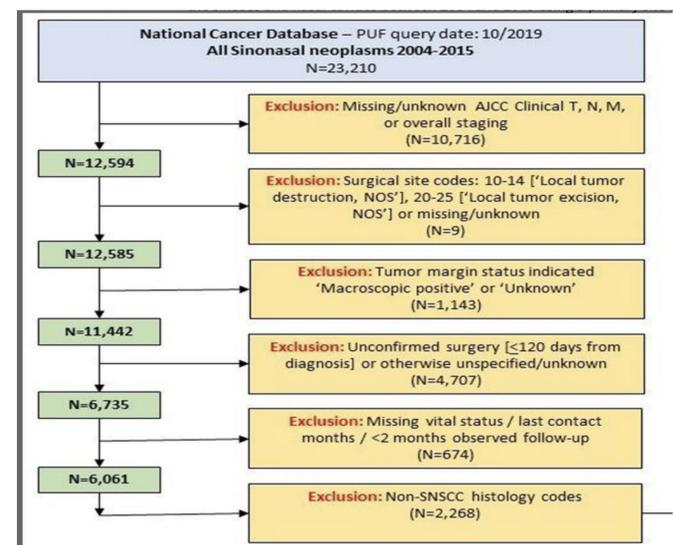
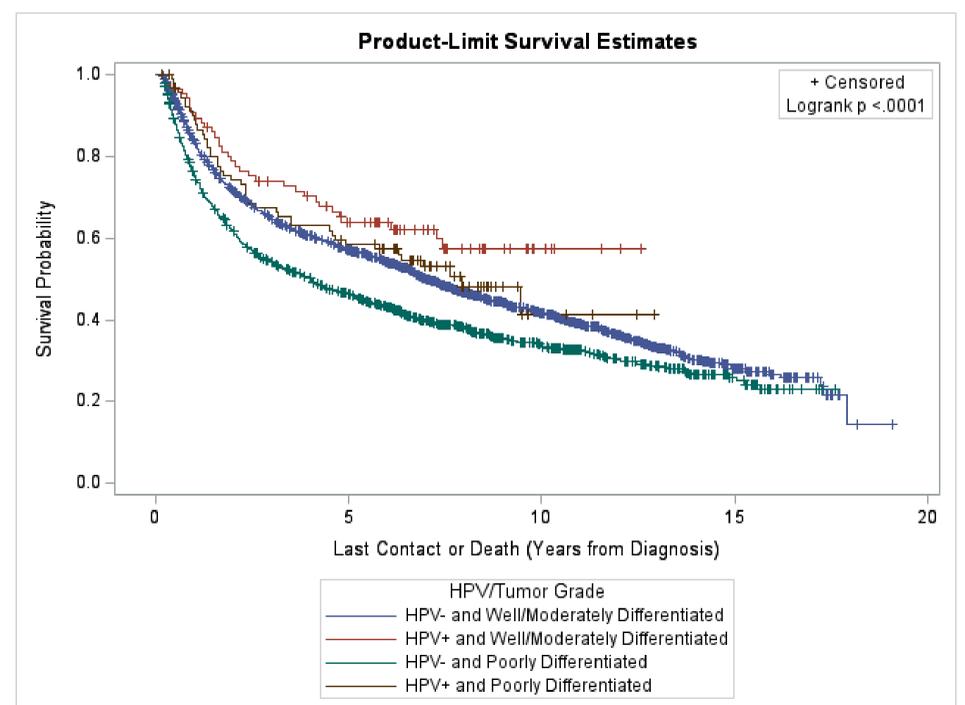


Figure 1: Kaplan-Meier Survival by HPV/Tumor Grade Status



Conclusions

- HPV status and tumor grade together have a significant impact on overall survival in sinonasal SCC, implying an interaction that affects prognosis.
- These results underscore the need for ongoing investigation into disease biology and support a careful, strategic approach to management.

Contact

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