

The role of p16 expression in response to induction chemotherapy in sinonasal malignancies

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Background

- Patients with p16-positive oropharyngeal squamous cell carcinoma (OPSCC) have a more favorable clinical outcome, with improved overall survival and enhanced responsiveness to systemic therapies, compared to their p16-negative counterparts.
- Although, some studies have shown p16 overexpression is associated with better overall survival in SNSCC, the clinical significance of p16 expression in sinonasal squamous cell carcinoma (SNSCC) is not well understood.
- Given the role of induction chemotherapy (IC) in the management of advanced-stage sinonasal carcinoma, particularly in tumors that are unresectable or locally advanced, the current study aims to assess the relationship between p16 expression and treatment response in this cohort.

Methods

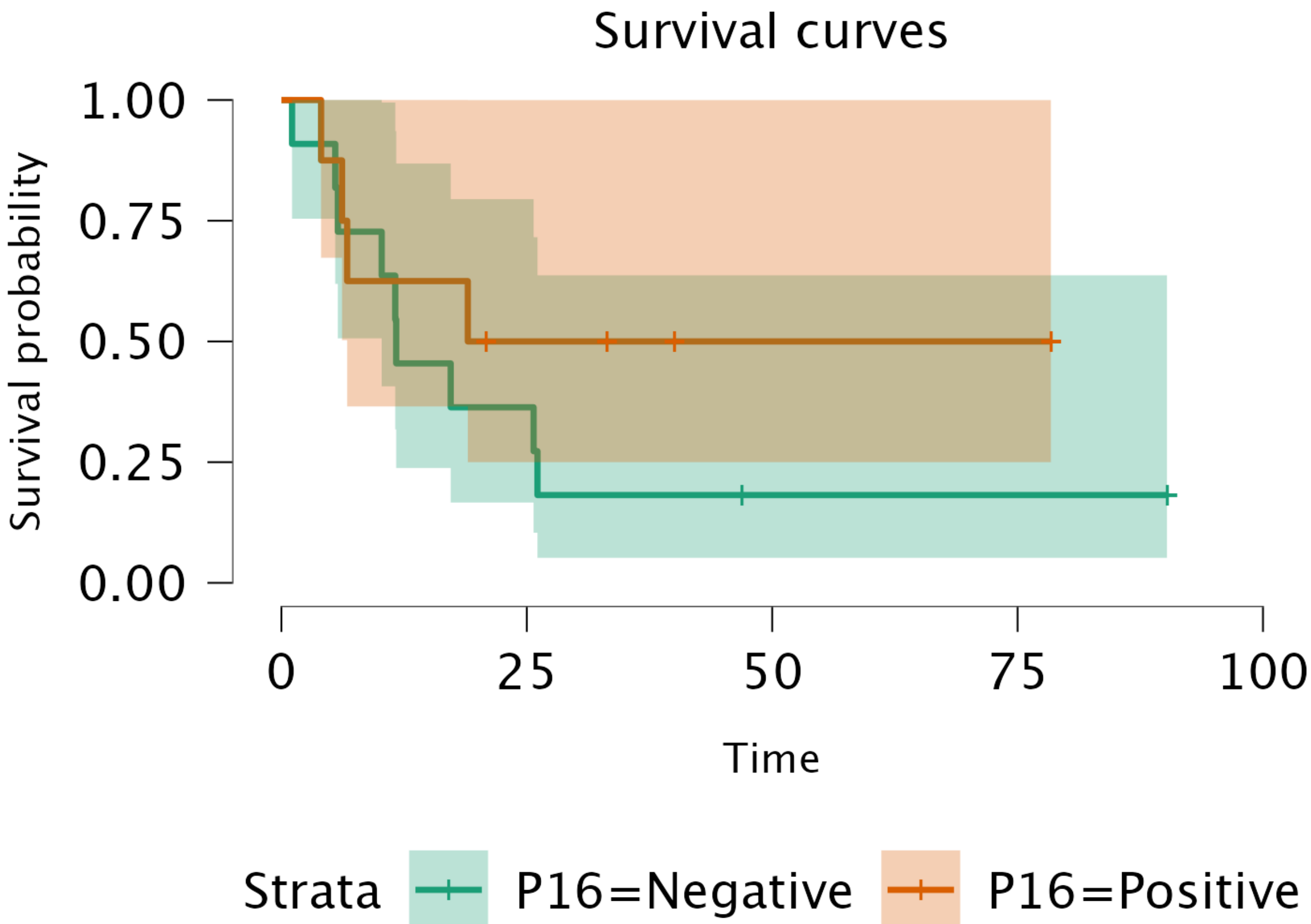
- Retrospective chart review was performed among treatment naïve adult patients who received induction chemotherapy for sinonasal carcinoma at a single institution between July 2010 and February 2019.
- Patients without p16 testing performed on pathology were excluded.
- Pre and post-imaging studies were evaluated and tumor volume measured according to the RECIST1.1 guidelines (See Figure 1) to evaluate tumor response to IC.
- Progression free survival rates were also calculated using Kaplan-Meier survival curves. Categorical comparisons were made using a Chi-square test.

Results

- 19 patients with advanced sinonasal carcinomas who underwent induction chemotherapy were included in this study.
- There was no statistical difference in response to induction chemotherapy between patients with p16 positive and p16 negative sinonasal carcinoma (62.5% with a favorable response vs 72.7% respectively, $p=0.912$).
- There was no statistically significant difference in progression free survival among patients with p16+ tumors and p16- tumors (median = 18.9 months vs 11.7 months respectively, $p=0.3$ (see Figure 2 for Kaplan-Meier Survival Curve).
- 36% of p16 negative tumors were noted to have dural involvement compared to 87.5% of p16 positive tumors ($p=0.059$) (see Figure 3).

Response	Criteria
Complete response (CR)	No remaining target lesions and reduced lymph node size to <10 mm
Partial response (PR)	At least 30% reduction in sum of target lesion diameters from baseline
Progressive disease (PD)	Absolute increase of at least 5 mm with increased sum of diameters of target lesions by 20% compared to the smallest baseline lesion, or appearance of new lesions
Stable disease (SD)	Inadequate change in size to qualify for PR or PD

Figure 1: RECIST1.1 guidelines: A CR or PR to induction chemotherapy was considered favorable, while SD and PD were considered unfavorable.



Kaplan-Meier Summary Table

Strata	N	Events	Restricted Mean	Standard Error	Median Survival
p16/HPV status=Negative	11	9	26.845	9.284	11.696
p16/HPV status=Positive	8	4	49.598	14.436	18.990

Tests Table

Test	Chi Square	df	p
Log-rank (Mantel-Haenszel)	1.072	1	0.300

Figure 2: Kaplan Meier Survival Curve demonstrating progression free survival among patients with p16 negative and p16 positive tumors

p16/HPV status	Dura involvement		Total
	0	1	
Negative	7	4	11
Positive	1	7	8
Total	8	11	19

Fisher's exact test	Log Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
	2.359	-0.157	6.439	0.059

Figure 3: Table comparing dural involvement between p16 negative and p16 positive tumors

Conclusions

- P16 Expression does not appear to be a prognostic indicator for overall response to induction chemotherapy.
- Furthermore, p16 expression did not significantly impact overall progression free survival in this study.
- A larger patient cohort is necessary to further elucidate the prognostic implications, if any, of p16 expression in patients with sinonasal carcinoma.

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