

## Abstract

**Introduction:** P16INKa (p16) positivity in head and neck squamous cell carcinomas (HNSCCs) has been shown to correlate with an overall improved prognosis. However, within this population there remains a subset of patients that experience relentless disease progression. It is our objective to further characterize p16 positive HNSCCs in an attempt to better predict patient outcomes.

**Methods:** A retrospective cohort review was performed at a single tertiary care center. A total of 105 patients were identified to have p16 positive tumors of the head and neck between May 5<sup>th</sup>, 2003 and August 5<sup>th</sup>, 2014

**Results:** A total of 104 patients were included in the final analysis. Mean follow up was 13 months. 19 patients presented with a history of recurrence following initial treatment with chemoradiation. The most common primary site was the oropharynx, followed by oral cavity. Overall, 2-year recurrence free survival was 81%. Multivariate Cox-regression analysis revealed that initial presentation with neck disease ( $p = 0.048$ ) and recurrence after failed chemoradiation ( $p = 0.014$ ) were independent predictors of recurrence.

**Conclusion:** Although p16 positivity in HNSCs is traditionally thought to indicate improved outcomes we have identified specific patient characteristics associated with aggressive disease; further investigation into this stratification is warranted.

## Introduction

P16INKa (p16) positivity in head and neck squamous cell carcinomas (HNSCCs) has been shown to indicate a favorable prognosis. However, within this population there remains a subset of patients that experience relentless disease progression. Now that treatment de-intensification protocols are beginning to be used in common practice, identifying and describing this population with poor response is critical. It is our objective to further characterize p16 positive HNSCCs in an attempt to better predict patient outcomes.

Demographic Data	Mean	Range
Age	62.5	33-85
Sex	%	n=
Male	77%	80
Female	23%	24
Race	%	n=
White	77%	80
Asian	4%	4
Hispanic	12%	12
Other	7%	7
Tobacco	43%	45
Alcohol	49%	51
T stage	%	n=
T1	24%	25
T2	44%	45
T3	20%	21
T4	12%	12
Perineural invasion	44%	45
Lymphovascular invasion	12%	12

Univariate Analysis for Recurrence	P value
Age	0.004
Lymphovascular Invasion	0.007
Concurrent Chemoradiation	0.034
Salvage Surgery	0.006
T stage	0.41
Grade	0.61
Perineural invasion	0.34
Race	0.89

## Time to recurrence in p16 positive head and neck squamous cell carcinoma

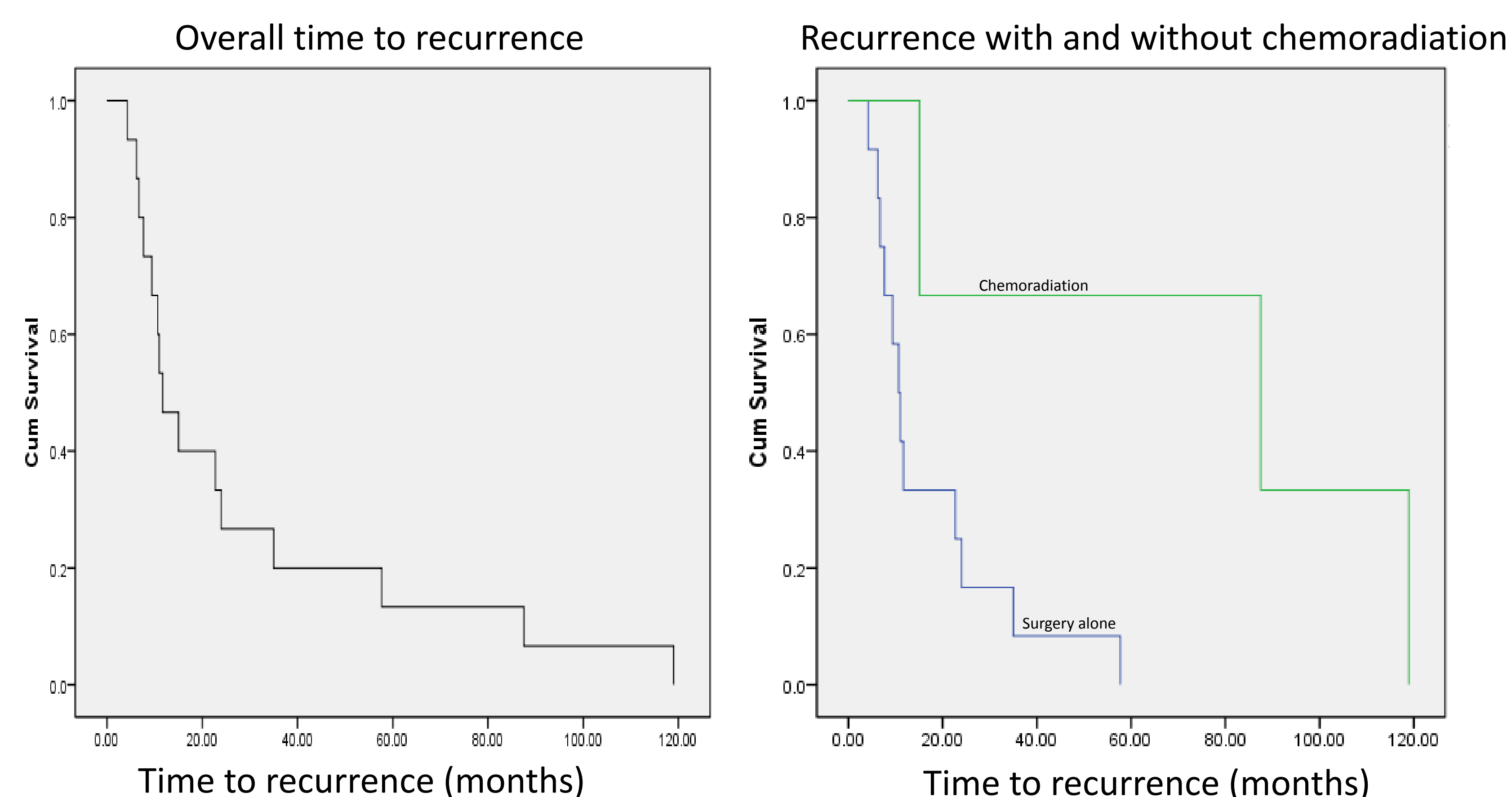


Figure 1 describes univariate analysis findings for all 104 patients investigated in the study. Numerous variables were found to correlate with disease recurrence: age, lymphovascular invasion, concurrent chemoradiation and salvage surgery. T stage, grade, perineural invasion and race did not. Multivariate analysis was performed showing that patients with neck disease at initial presentation and with a history of failed chemoradiation had higher chance of recurrence.

## Results

A total of 104 patients were included in the final analysis. Mean follow up was 13 months. 19 patients presented with a history of recurrence following initial treatment with chemoradiation. The most common primary site was the oropharynx, followed by oral cavity. Overall, 2-year recurrence free survival was 81%. Multivariate Cox-regression analysis revealed that initial presentation with neck disease ( $p = 0.048$ ) and recurrence after failed chemoradiation ( $p = 0.014$ ) were independent predictors of recurrence.

## Discussion

P16 positivity has been established to play a part in the pathogenesis and disease process of a large subset of head and neck squamous cell carcinomas.

Numerous publications have been published supporting that p16 and the related squamous cell carcinomas are associated with improved clinical outcomes with reduced risks of recurrence.

However, there remains a subset of patients, that despite their p16 positivity, are subject to aggressive disease progression and poor overall outcomes.

Our analysis shows that, of patients with p16 positive head and neck squamous cell carcinomas, those presenting with neck disease or after failed chemoradiation will most likely recur and have outcomes similar to non-p16 related disease. Univariate analysis also indicates that overall recurrence was associated with lymphovascular invasion ( $p = 0.007$ ). Perineural invasion, tobacco / alcohol history, and T stage did not have any impact on survival nor did it correlate to recurrence.

## Conclusions

Although p16 positivity in HNSCs is traditionally thought to indicate improved outcomes we have identified specific patient characteristics associated with aggressive disease; further investigation into this stratification is warranted.

## References

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