

What factors predict prognosis in OPSCC patients with complete treatment response?

R Grant Muller MD^{1,2}, Chelsea S Hamill MD^{1,2}, Brandon Vu BS², Jason E Thuener MD^{1,2}, Jay Wasman MD^{1,2}, Shawn Li MD^{1,2}, Nicole M Fowler MD^{1,2}, Rod P Rezaee MD^{1,2}, Pierre Lavertu MD^{1,2}, Theodoros N Teknos MD^{1,2}, Quintin Pan PhD^{1,2}, and Wendi Q O'Neill MS, DDS²

¹ Ear, Nose, and Throat Institute, University Hospitals Cleveland Medical Center, *Cleveland, OH*

² Case Western Reserve University School of Medicine, *Cleveland, OH*

INTRODUCTION

Oropharyngeal squamous cell carcinoma (OPSCC) has two presentations – classically, older males with longstanding tobacco use and, more recently, younger males with human papillomavirus (HPV) infection. HPV+ OPSCC is rising and associated with improved prognosis and treatment response.

Curative treatment, regardless of HPV status, primarily involves various combinations of modalities centered around primary surgery versus radiotherapy. Numerous factors influence treatment choice including: patient comorbidities, clinicopathologic characteristics, national consensus guidelines and multidisciplinary discussion.

However, the independent impact of both pre-treatment factors (e.g. staging) and treatment factors (e.g. modality, treatment response) remains to be fully elucidated within this patient population.

METHODS

A single institution retrospective study was performed.

We included patients from 2007 to 2018 diagnosed with OPSCC that underwent curative treatment with complete response (CR). CR was defined as negative clinical examination and/or imaging 3 months post-treatment.

p16 was used as a surrogate for HPV+ status.

Kaplan-Meier curves, and multivariate analysis were used to evaluate the effects of treatment responses, AJCC 8th edition overall stage, and treatment modality on 5-year overall survival (OS).

	p16- (n=74)	p16+ (n=230)	Total (n=304)	p value
Age, mean (SD)	63.5 (10.6)	61.1 (9.5)	61.7 (9.8)	0.07
Gender, n (%)				
Female	20 (27.0)	41 (17.8)	61 (20.1)	0.09
Male	54 (73.0)	189 (82.2)	243 (79.9)	
Smoking Status, n (%)				0.01
No	12 (16.2)	81 (35.2)	93 (30.6)	
Yes	58 (78.4)	144 (62.6)	202 (66.4)	
Unknown	4 (5.4)	5 (2.1)	9 (2.9)	
Subsite, n (%)				0.01
Tonsil	28 (37.8)	110 (48.0)	138 (45.5)	
BOT	28 (37.8)	96 (41.9)	124 (40.9)	
OP	18 (24.3)	23 (10.0)	41 (13.5)	

Table 1: Patient demographics of our cohort. Patients with p16+ OPSCC were less likely to smoke and more likely to present with tonsil primaries.

	p16- (n=74)	p16+ (n=230)	Total (n=304)	p value
T Stage, n (%)				0.01
T1/T2	36 (50.0)	152 (67.0)	188 (62.9)	
T3/T4	36 (50.0)	75 (33.0)	111 (37.1)	
N Stage, n (%)				<0.001
N0	32 (43.2)	33 (14.3)	65 (21.4)	
N1	29 (39.2)	157 (68.3)	186 (61.2)	
N2	11 (14.9)	32 (13.9)	43 (14.1)	
N3	0 (0)	5 (2.2)	5 (1.6)	
Overall Stage, n (%)				<0.001
I	5 (6.8)	138 (60.0)	143 (47.0)	
II	13 (17.6)	68 (29.6)	81 (26.6)	
III	11 (14.9)	21 (9.1)	32 (10.5)	
IV	43 (58.1)	0 (0.0)	43 (14.1)	

Table 2: Clinicopathologic characteristics of our cohort. Patients with p16+ OPSCC were more likely to present with less advanced primary tumors and overall stage but higher nodal disease.

RESULTS

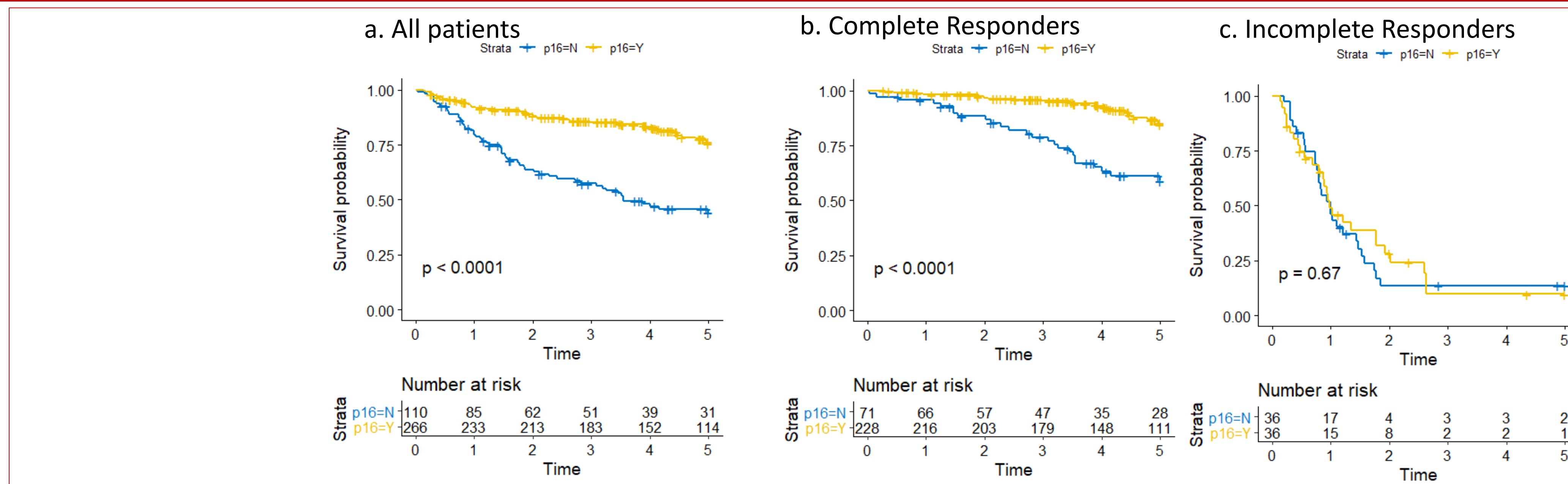


Figure 1a-c. 5-year OS stratified by p16 status in entire cohort (a), complete responders (b), and incomplete responders (c). p16+ status is associated with improved OS in CRs but not IRs

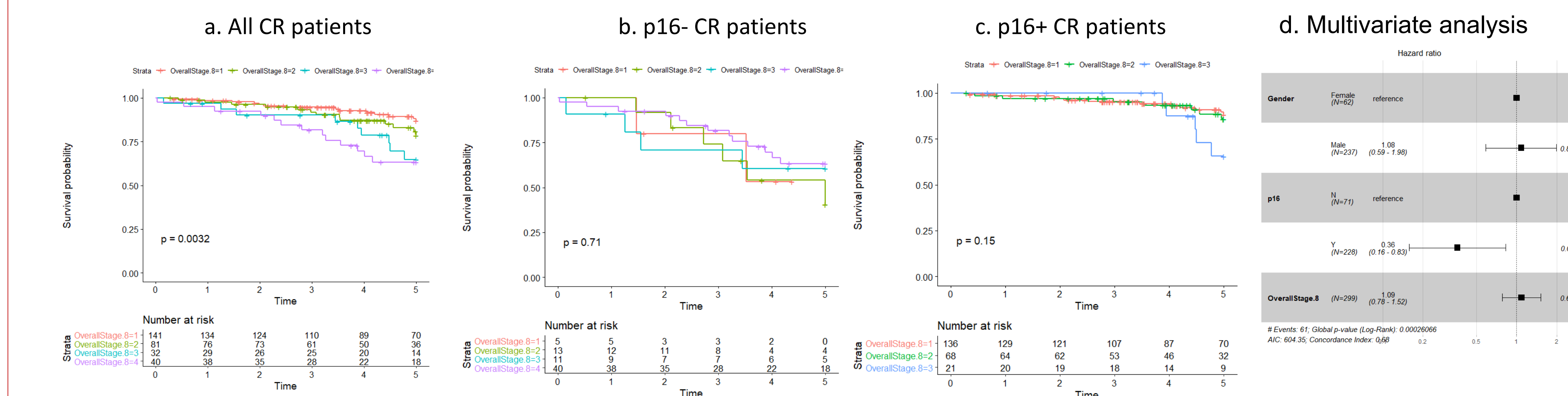


Figure 2a-d: 5-year OS stratified by AJCC 8th edition overall stage in all CR patients (a), p16- CR (b), and p16+ CR. OS is not influenced by AJCC 8th edition in CRs with p16+ or p16- OPSCC. Multivariate analysis (d) showed that p16+ status but not overall stage is an independent predictor of 5-year OS.

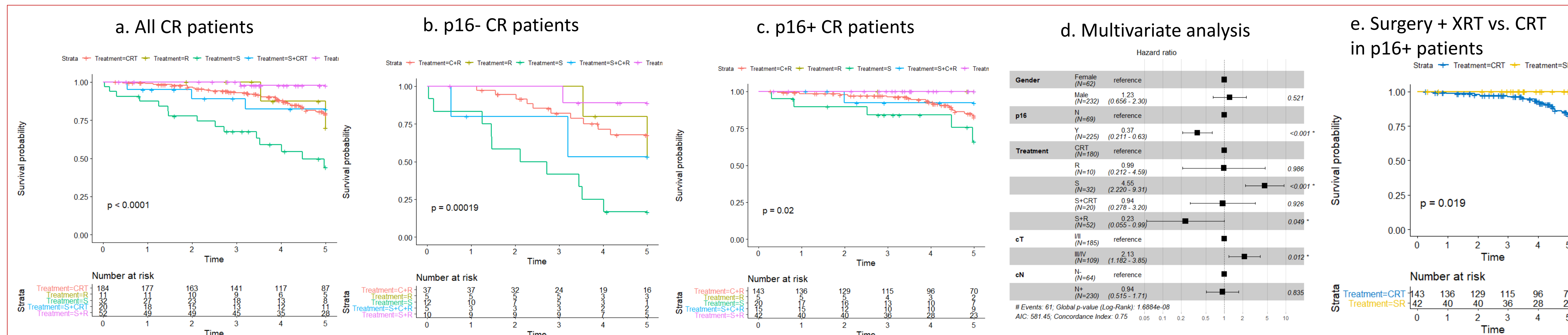


Figure 3a-e: 5-year OS stratified by treatment modality in all CR patients (a), p16- CR (b), and p16+ CR. Across all cohorts, surgery alone was associated with decreased OS. (d) Multivariate analysis showed that p16 status, surgery, surgery + XRT, and late T stage are all independent predictors of survival. (e) In p16+ patients, surgery + XRT is associated with greater OS compared to CRT.

CONCLUSIONS

- p16+ status is a favorable independent prognostic indicator in patients with OPSCC with complete treatment response but not in those with incomplete treatment response.
- Overall staging by the AJCC 8th edition does not predict overall survival in patients with complete response, irrespective of p16 status.
- Surgery + XRT is superior to CRT in 5-year overall survival in p16+ patients with complete response.
- Prospective trial and other considerations, including disease free survival and functional outcomes, must be investigated.

REFERENCES

- National Comprehensive Cancer Network. Head and Neck Cancers (Version 1.2021). https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed December 27, 2020.
- Dayyani F, Etzel CJ, Liu M, et al. Meta-analysis of the impact of human papillomavirus (HPV) on cancer risk and overall survival in head and neck squamous cell carcinomas (HNSCC) Head Neck Oncol 2010;2:15.
- Amin MB, Edge S, Greene F, Byrd DR, et al. AJCC Cancer Staging Manual (8th Edition). Spring International Publishing: American Joint Commission on Cancer; 2017.

*Corresponding author:

R Grant Muller, MD

University Hospitals Cleveland Medical Center

11100 Euclid Avenue (LKS 4518)

Cleveland, OH 44106

E-mail : Richard.muller@UHhospitals.org