

Prognostic Impact of HPV Status and Disease-Free Interval in Salvage Surgery for Oropharyngeal Squamous Cell Carcinoma



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INTRODUCTION

- Overall survival (OS) for salvage surgery in recurrent oropharyngeal squamous cell carcinoma (OPSCC) is historically poor
- Short or no disease-free interval (DFI) between completion of primary therapy and recurrence has previously been shown to be predictive of poor survival in head and neck squamous cell carcinoma
- Human papilloma virus status previously shown to be a strong predictor of OS in primary treatment of OPSCC as well as in setting of disease progression
- Hypothesis:** patients with P16(+) OPSCC and longer DFI (>6 months) after primary therapy will have better survival outcomes in the salvage setting compared to patients with P16(-) tumors or short DFI (≤6 months)

METHODS

- Multi-institutional retrospective chart review from January 1, 2002-December 31, 2018
- Adult patients greater than 18 years old who underwent salvage surgery for recurrent OPSCC were included
- Patients excluded were those who 1) underwent salvage surgery with benign pathology results, 2) underwent primary surgery for new oropharyngeal malignancy after radiation with or without chemotherapy in a separate head and neck subsite, or 3) had distant metastatic disease at the time of initial or salvage treatment
- All tumors were staged according to American Joint Committee on Cancer 7th edition
- Primary Outcome** was 3-year and 5-year OS after salvage therapy by P16 status
- Secondary Outcome** was 3-year and 5-year OS by DFI
- Univariate analyses performed with Chi-square, Fisher exact, and two-tailed student *t*-test where indicated
- Kaplan-Meier survival analyses performed using log-rank test
- All statistical analyses performed using Graphpad Prism 8, and statistical significance was assessed with an alpha level of 0.05.

RESULTS

Table 1. Descriptive Data				
Variable	All, N (%)	P16-Positive, N (%)	P16-Negative, N (%)	p Value
Total Patients	90	27 (30)	23 (26)	
Mean age at presentation, y	64	63.6±7.4	65.1±10.2	0.6
Sex				
Male	58 (64)	17 (63)	10 (43)	0.03
Female	17 (19)	2 (7)	8 (35)	0.03
Comorbidity				
Diabetes	4 (4)	2 (7)	0	-
Hypertension	22 (24)	5 (19)	12 (52)	0.02
Cardiac disease	6 (7)	2 (7)	1 (4)	>0.9
Pulmonary disease	6 (7)	0	5 (22)	-
Mean pack year history, y	32.7	23.4±24.8	37.9±18.9	0.04
Alcohol use history	67 (74)	19 (70)	19 (83)	0.3
Initial disease				
Tumor site				
Tonsil	47 (52)	14 (52)	14 (61)	0.6
Base of tongue	39 (43)	12 (44)	8 (52)	0.6
Soft palate	3 (3)	1 (4)	1 (4)	>0.9
Posterior Pharyngeal Wall	1 (1)	0	0	-
Tumor classification				
T1-T2	45 (50)	14 (52)	11 (48)	>0.9
T3-T4	40 (44)	13 (48)	9 (39)	>0.9
Nodal stage				
N0	18 (20)	3 (11)	6 (26)	0.3
N1	17 (19)	6 (22)	3 (13)	0.5
N2a	8 (9)	0	4 (17)	-
N2b	20 (22)	9 (33)	5 (22)	0.4
N2c	14 (16)	6 (22)	2 (9)	0.3
N3	6 (7)	0	1 (4)	-
Overall disease stage				
I-II	9 (10)	2 (7)	4 (17)	0.4
III-IV	73 (81)	25 (93)	16 (70)	0.4
Primary Treatment				
Radiotherapy	21 (23)	5 (19)	6 (22)	0.5
Chemoradiotherapy	67 (74)	22 (81)	16 (59)	0.5
Surgery + Chemoradiotherapy	1 (1)	0	0	-

Table 2. Patterns of Recurrence & Treatment				
Variable	All, N (%)	P16-Positive, N (%)	P16-Negative, N (%)	p Value
Disease-Free Interval				
≤6 months	52 (58)	11 (41)	11 (48)	0.8
>6 months	37 (41)	16 (59)	12 (52)	0.8
Local Recurrence				
Base of Tongue	58 (62)	16 (59)	17 (74)	0.4
Tonsil	19 (33)	6 (38)	3 (13)	0.3
Posterior pharyngeal wall	30 (52)	9 (56)	11 (48)	0.7
Soft Palate	2 (4)	0	1 (4)	-
Other*	5 (10)	1 (6)	3 (13)	0.6
Other*	2 (4)	0	1 (4)	-
Regional Recurrence	47 (52)	16 (59)	10 (43)	0.4
Treatment				
Open	42 (47)	11 (41)	10 (43)	>0.9
Robotic	16 (18)	5 (19)	8 (35)	0.2
Neck Dissection	79 (88)	22 (81)	20 (87)	0.7
Free Tissue Transfer	12 (13)	6 (22)	5 (22)	>0.9
Regional Flap	4 (4)	0	3 (13)	-
Pathologic tumor classification				
pT1-pT2	37 (64)	11 (41)	12 (52)	0.4
pT3-pT4	13 (22)	1 (4)	5 (22)	0.4
Neck disease				
pN-	33 (42)	5 (19)	11 (48)	0.1
pN+	46 (58)	16 (59)	10 (43)	0.1
Margin Status				
Positive	11 (12)	1 (4)	4 (17)	0.2
Negative	64 (71)	23 (85)	16 (70)	0.2
Adjuvant Therapy				
Reirradiation	3 (4)	1 (4)	0	-
Chemoreirradiation	10 (13)	3 (11)	6 (26)	0.3

Table 3. Recurrence & Quality of Life After Salvage				
Variable	All, N (%)	P16-Positive, N (%)	P16-Negative, N (%)	p Value
Recurrent/Residual Disease	44 (49)	14 (52)	18 (78)	0.08
Reirradiation	9 (10)	2 (7)	2 (9)	>0.9
Chemoreirradiation	8 (9)	4 (15)	3 (13)	0.7
Palliative Chemotherapy	14 (16)	2 (7)	7 (30)	0.2
Repeat Salvage Surgery	13 (14)	4 (15)	3 (13)	0.7
Subsequent Hospice	11 (12)	3 (11)	6 (26)	0.7
Tracheostomy Dependence	24 (27)	8 (30)	7 (30)	>0.9
Gastrostomy Dependence	39 (43)	12 (44)	14 (61)	0.3

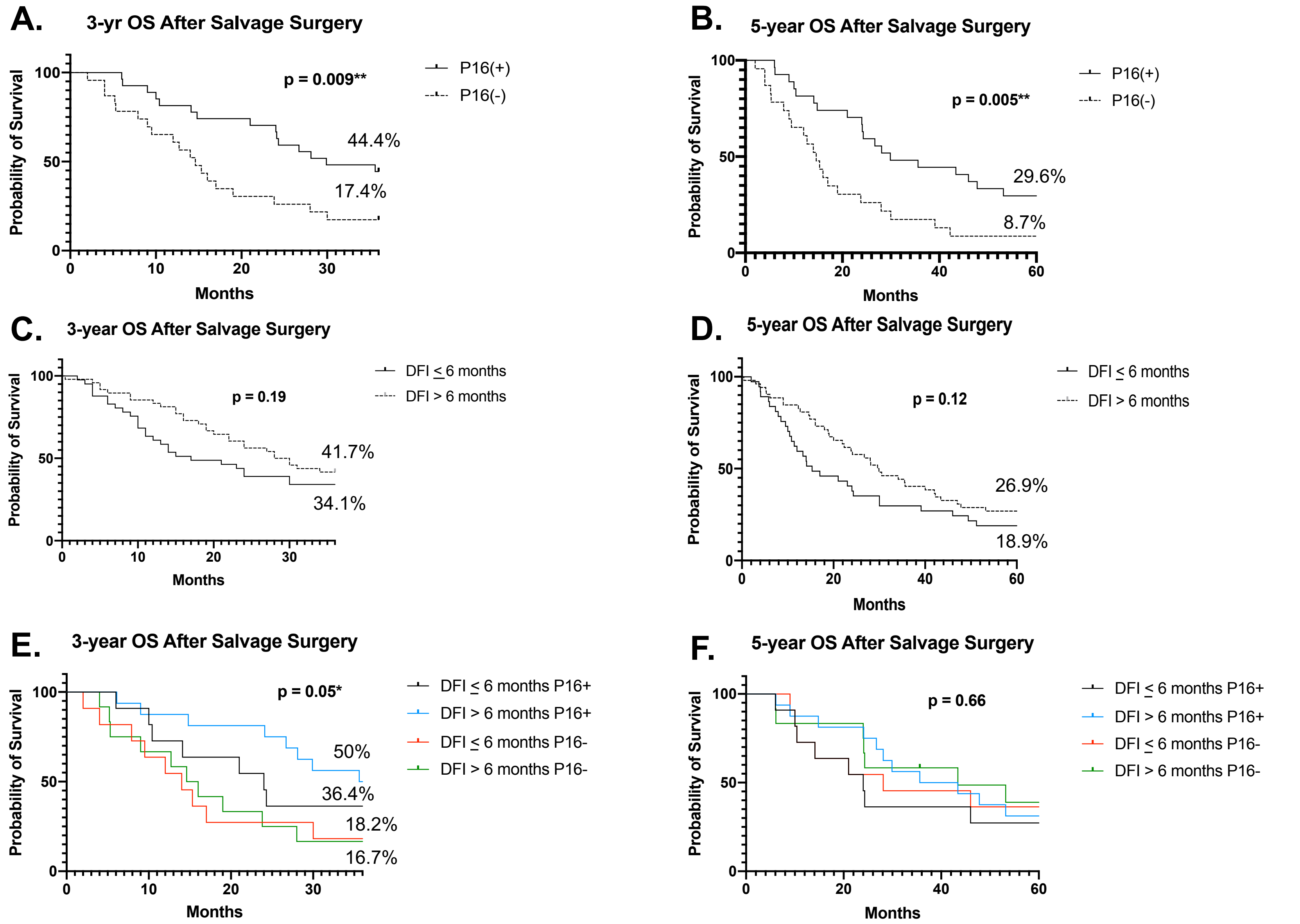


Fig 1. Kaplan-Meier survival analysis examining 3-year OS & 5-year OS by p-16 status (A&B), DFI (C&D), and P16 status stratified by DFI (E&F).

CONCLUSION

- P16 status impacts overall prognosis in salvage surgical setting for OPSCC
- P16-positive patients have better short-term prognosis regardless of DFI compared to P16-negative patients
- No significant difference in 5-year OS based upon DFI after salvage surgery

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References

- Fakhry C., Zhang Q., Nguyen-Tan P.F., et al. Human papillomavirus and overall survival after progression of oropharyngeal squamous cell carcinoma. *J Clin Oncol.* 2014
- Philouze P., Peron J., Poupart M., Pujo K., Buiet G., Ceruse P. Salvage surgery for oropharyngeal squamous cell carcinomas: A retrospective study from 2005 to 2013. *Head Neck.* 2017
- Zenga J., Graboyes E., Janz T., et al. Salvage of Recurrence after Surgery and Adjuvant Therapy: A Multi-institutional Study. *Otolaryngol Head Neck Surg.* 2019
- Zafereo M., Hanasono M.M., Rosenthal D.I., et al. The role of salvage surgery in patients with recurrent squamous cell carcinoma of the oropharynx. *Cancer.* 2009