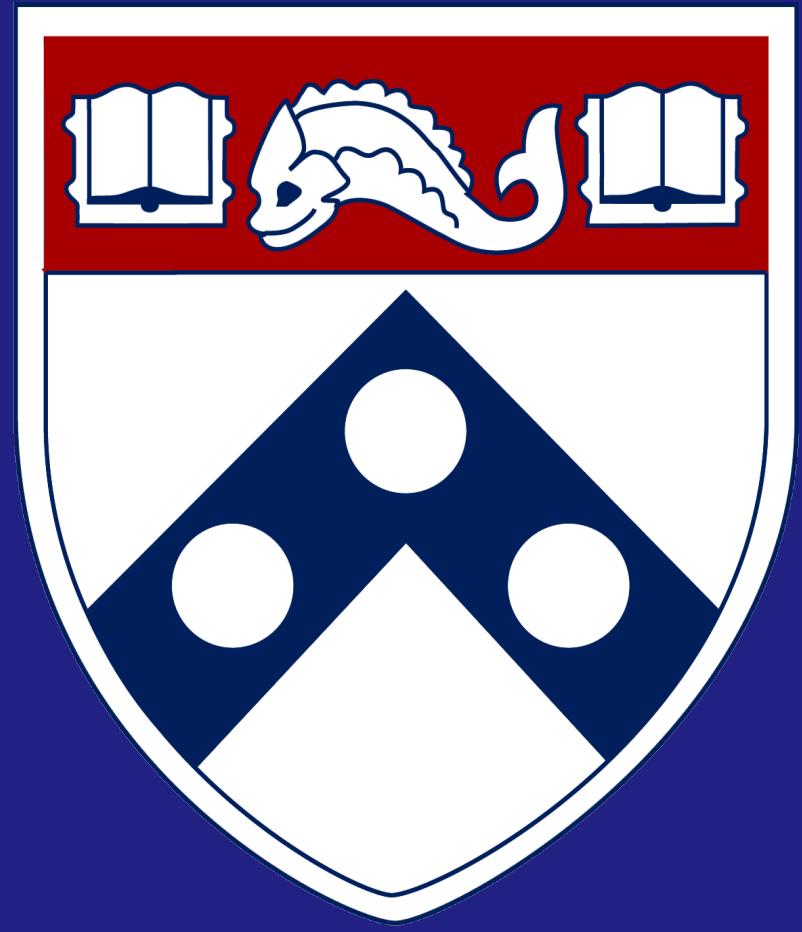




TREATMENT PARADIGMS AND SURVIVAL OUTCOMES FOR HPV-ASSOCIATED OROPHARYNGEAL CANCER PATIENTS USING THE NATIONAL CANCER DATABASE

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Introduction

- Human papillomavirus (HPV) represents a significant risk factor to the development of oropharynx squamous cell carcinoma (OPSCC). It is estimated that 40-80% of OPSCC cases are HPV-related [1,3].
- There is a 20% death rate in HPV+ OPSCC despite patients having higher survival probabilities compared to those with HPV- OPSCC [2].
- Current research addressing treatments for HPV-positive OPSCC is contradictory and lacks a clear consensus on the best treatment paradigm—while some studies advocate for treatment de-escalation, others propose a multimodal approach to increase survival probabilities [1,2].
- Objective: Given the lack of standardized treatment for HPV-related OPSCC, this retrospective study aims to use the National Cancer

Methods and Materials

- The National Cancer Database (NCDB) is a project co-sponsored by the Commission on Cancer (CoC) of the American College of Surgeons and the American College of Surgeons and the American Cancer Society. It is comprised of de-identified and unverified clinical surveillance data across 1500 CoC-accredited facilities and represents 70% of cancer cases throughout the United States.
- Data range from 2010-2015 and were selected based on codes derived from the International Classification of Defense for Oncology. Anatomic codes C090, C091, C098, C099, C100, C102, C103, C104, C108, C109, C019, and C024; histology codes 8070, 8071, 8072, 8076; behavior code ‘3,’ were selected for.
- Patients who did not have a positive HPV status were not considered. Cases were excluded if there were missing follow up and vital statuses, if patients received surgery to a distant site, is patients received palliative care or had missing value for this status, and if they received treatment across multiple centers.
- Patients who received radiation or chemoradiation as primary treatment and received non-standard dosage (<50 Gy or >70 Gy) were excluded from analysis.

- A total of 20,741 patients met inclusion criteria across 2010-2015. Demographic, tumor, and treatment characteristics for all subjects can be found in Table 1.
- The majority of patients received chemoradiation (44.1%), followed by surgery with adjuvant chemoradiation (22.1%), and surgery with adjuvant radiation (11.5%), as seen in Table 2.
- Unadjusted Kaplan-Meier overall survival based on varying treatment models is shown in Figure 1 alongside number at risk margins. While the majority of patients received chemoradiation, surgery with adjuvant chemoradiation or adjuvant radiation have better survival outcomes.

- In Table 2, univariate survival analysis shows that those who received surgery with adjuvant radiation have the best 3-year overall survival of 91.5% [95% CI: 90.3-92.8], and 5-year overall survival of 86.3% [95% CI: 84.2-88.3].

- In Table 3, multivariable cox proportional hazard analysis controlled for age, sex, race, insurance status, comorbidity score, facility type, facility location, and T and N stages, patients who received chemoradiation have worse

Table 1 - Subject Characteristics	n (%)
Total	20, 741
Age (Mean (SD))	58.99
Sex	
Male	17,748 (85.6)
Female	2,993 (14.4)
Race	
White	19,333 (93.2)
Black	917 (4.4)
Asian	184 (0.9)
Other/Unknown	307 (1.5)
Insurance status	
Private	12,503 (60.3)
Uninsured	684 (3.3)
Medicaid	1,270 (6.1)
Medicare	5,450 (26.3)
Other Government	489 (2.4)
Unknown	345 (1.7)
Comorbidity (Charlson-Deyo Score)	
0	17,301 (83.4)
1	2,650 (12.8)
2	571 (2.8)
3	219 (1.1)
Facility Type	
Community Cancer Program	1,276 (6.2)
Comprehensive Community Cancer Program	6,178 (29.8)
Academic/Research Program	10,502 (50.6)
Integrated Network Cancer Program	2,467 (11.9)
NA	318 (1.5)
Clinical T Stage	
T1	5,572 (26.9)
T2	8,207 (39.6)
T3	3,101 (15.0)
T4A	1,583 (7.6)
Clinical N Stage	
N0	2,752 (13.3)
N1	3,672 (17.7)
N2	1,531 (7.4)
N2A	1,970 (9.5)
N2B	6,827 (32.9)
N2C	2,725 (13.1)
N3	705 (3.4)
NX	559 (2.7)
Treatment Model	
Surgery with adjuvant chemoradiation	5,033 (24.3)
Surgery alone	1,514 (7.3)
Surgery with adjuvant radiation	2,388 (11.5)
Chemoradiation	9,157 (44.1)
Radiation alone	1,224 (5.9)
Other treatment	1,425 (6.9)

Results

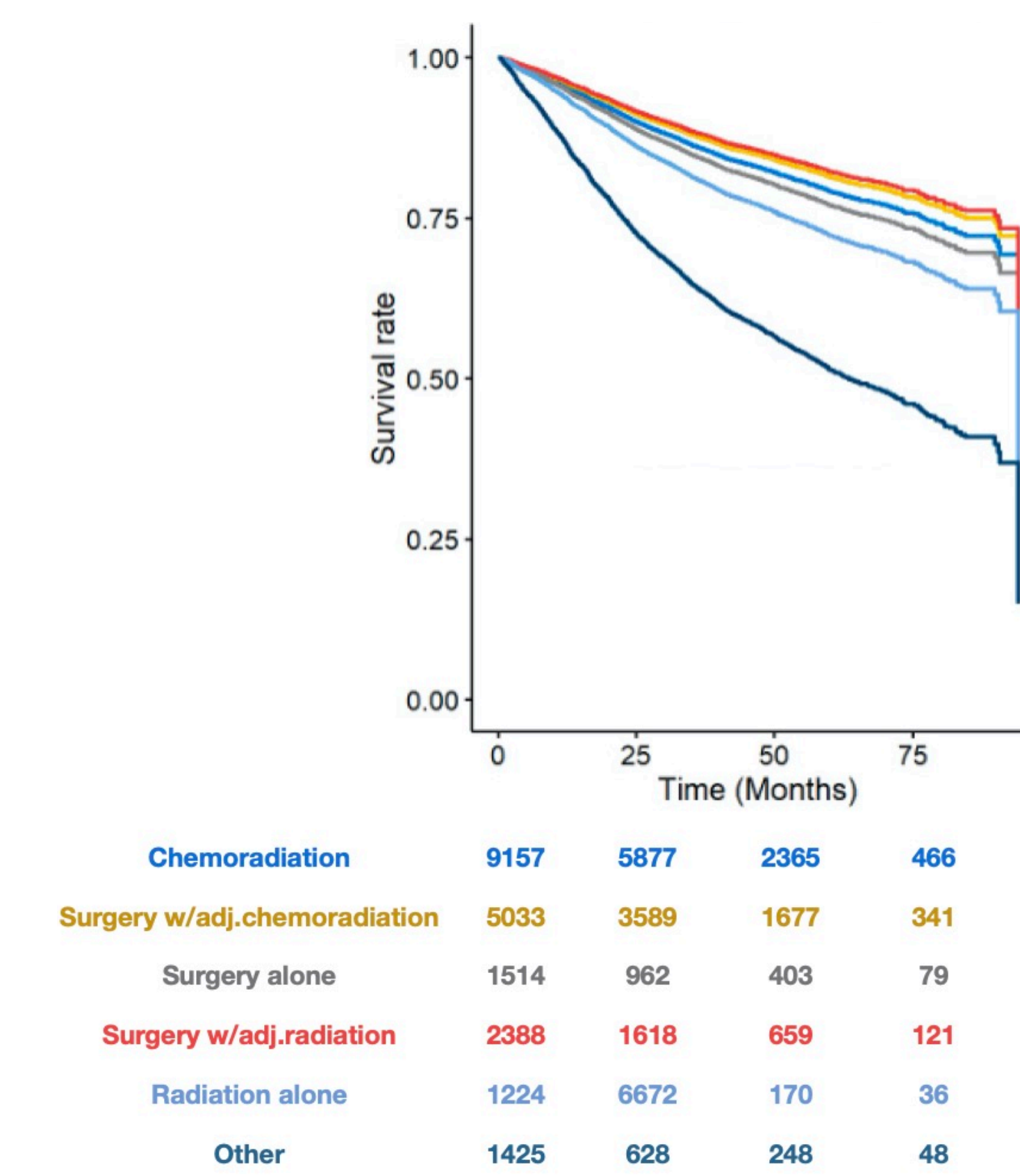


Fig.1 Unadjusted Kaplan-Meier overall survival curves for univariate analysis of treatment models.

Table 2 - Univariable Survival Analysis			
Treatment Model	1-year survival (%) [95% CI]	3-year survival (%) [95% CI]	5-year survival (%) [95% CI]
All	95.0% [94.7-95.3]	84.8% [84.2-85.3]	77.9% [77.1-78.7]
Surgery with adjuvant chemoradiation	97.7% [97.2-98.1]	90.8% [90.0-91.7]	85.2% [83.9-86.6]
Surgery alone	95.5% [94.5-96.6]	88.0% [86.2-89.9]	82.0% [79.3-84.8]
Surgery with adjuvant radiation	97.8% [97.2-98.4]	91.5% [90.3-92.8]	86.3% [84.2-88.3]
Chemoradiation	95.8% [95.4-96.3]	83.8% [82.9-84.7]	75.5% [74.3-76.8]
Radiation alone	92.8% [91.3-94.3]	76.9% [74.1-79.8]	65.7% [61.3-70.5]
Other treatment	76.9% [74.6-79.2]	59.7% [56.9-62.6]	54.7% [51.6-58.0]

Table 3 - Multivariable Cox proportional hazard analysis - Model controlled for sex, race, age, comorbidity score, insurance status, facility type, facility location, and T and N stages.		
Treatment Model	HR [95% CI]	P value
Chemoradiation	1	
Surgery alone	1.13 [0.96-1.34]	0.15
Surgery with adjuvant radiation	0.82 [0.71-0.96]	<0.05
Surgery with adjuvant chemoradiation	0.87 [0.79-0.97]	<0.05
Radiation alone	1.43 [1.25-1.65]	<0.0005
Other treatment	3.29 [2.97-3.64]	<0.0005

- worse survival outcomes compared to those who received surgery with adjuvant radiation or adjuvant chemoradiation (HR, 0.82, [95% CI: 0.71-0.96], HR, 0.87, [95% CI: 0.79-0.97], respectively).
- There is no significant difference between the survival probabilities of those who received surgery with adjuvant chemoradiation and adjuvant radiation (HR, 1.09, [95% CI:0.90-1.25]).

Discussion

- This retrospective study showed that majority of patients diagnosed with HPV+ OPSCC receive chemoradiation as primary treatment.
- Multivariable analysis of NCDB data showed that chemoradiation does not have the overall advantage. Surgery followed by chemoradiation or surgery followed by radiation result in better survival probabilities.

Significance

- There is currently minimal research on the treatment efficacies for HPV+ OPSCC that encompasses all disease stages. This study shows despite chemoradiation being the most used treatment, surgery with adjuvant chemoradiation or adjuvant radiation yield the best survival outcomes.
- This finding suggest a need to shift to a multimodal approach from the current chemoradiation approach.