

PROGNOSTIC SIGNIFICANCE OF HUMAN PAPILLOMA VIRUS (HPV) IN PENILE CANCER: A NATIONAL CANCER DATABASE (NCDB) STUDY

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BACKGROUND

- Penile cancer is a relatively rare tumor in developed nations.
- HPV is associated with 30 - 50% of penile cancers, with some studies showing improved outcomes in these patients.
- In this study, we have evaluated the effect of HPV infection on the outcomes of penile cancer utilizing a contemporary national cancer database (NCDB).

METHODS

- The NCDB was utilized to identify penile cancer patients who were tested for HPV at the time of diagnosis from 2004 – 2016.
- Chi-squared were used to compare HPV positive and negative patients.
- Cox regression models were used to assess the effect of patient and treatment factors on overall survival.

BASELINE CHARACTERISTICS

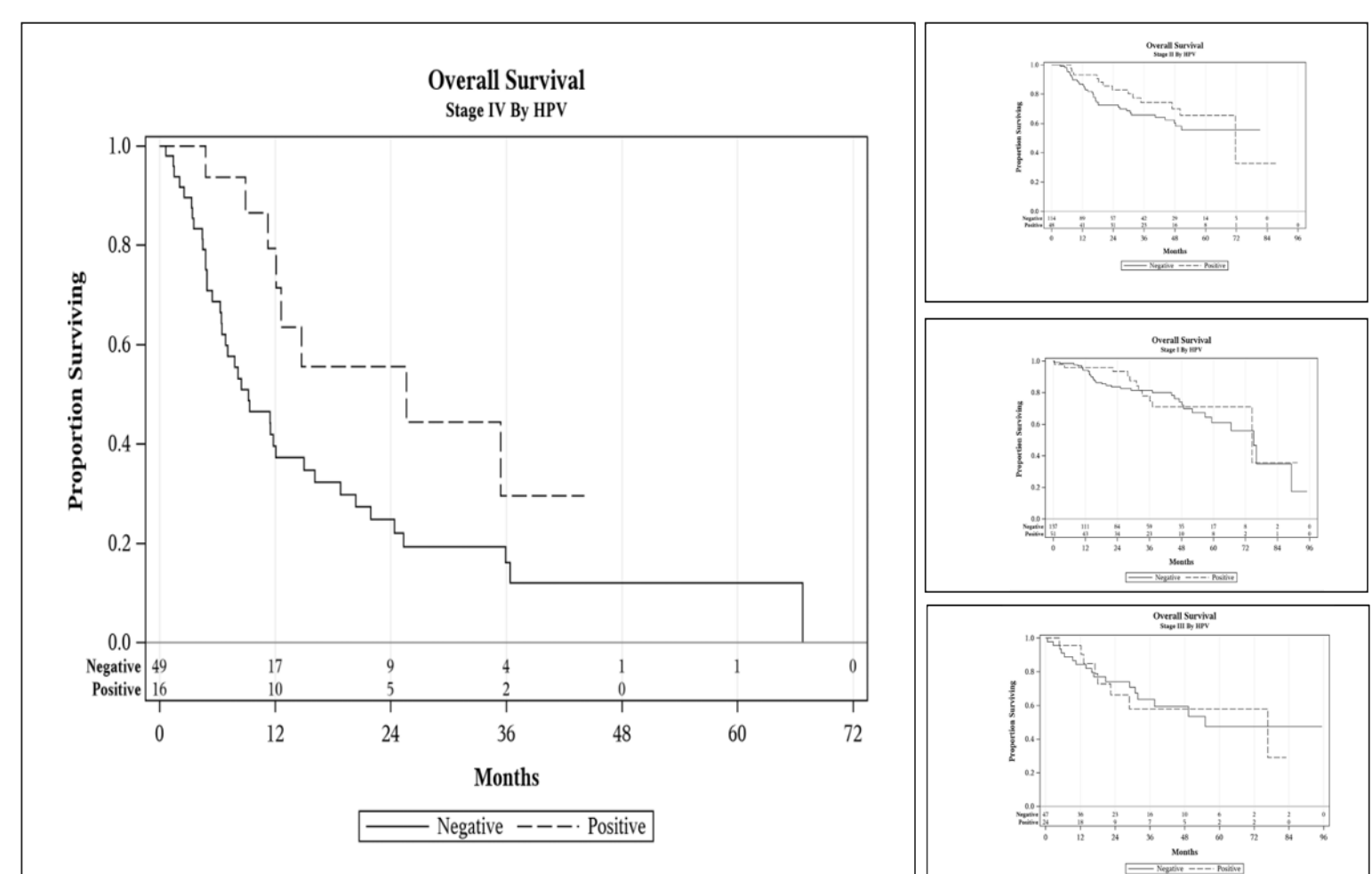
Covariate	Level	Overall N=486	HPV		P-value
			Negative N=347	Positive N=139	
Facility Type	Academic	251 (55)	182 (56.7)	69 (51.1)	0.27
	Non-academic	205 (45)	139 (43.3)	66 (48.9)	
	Missing	30	26	4	
Facility Location	Central	158 (34.6)	108 (33.6)	50 (37)	0.77
	Mountain & Pacific	78 (17.1)	55 (17.1)	23 (17)	
	New England & Atlantic	220 (48.2)	176 (50.7)	64 (46)	
	Missing	30	26	4	
Cases For Year of Diagnosis	<5 cases	332 (68.3)	240 (69.2)	92 (66.2)	0.52
	5+ cases	154 (31.7)	107 (30.8)	47 (33.8)	
Age	<65	246 (50.6)	171 (49.3)	75 (54)	0.35
	65+	240 (49.4)	176 (50.7)	64 (46)	
Race \ Ethnicity	Black	50 (10.4)	32 (9.3)	18 (12.9)	0.15
	Hispanic	73 (15.1)	50 (14.5)	23 (16.5)	
	Other	26 (5.4)	23 (6.7)	3 (2.2)	
	White	334 (69.2)	239 (69.5)	95 (68.3)	
	Missing	3	3	0	
Primary Payor	Not insured	35 (7.3)	29 (8.5)	6 (4.4)	0.30
	Private	152 (31.9)	109 (31.9)	43 (31.9)	
	Public	290 (60.8)	204 (59.6)	86 (63.7)	
	Missing	9	5	4	
Median Income Quartiles 2008-2012	<\$48,000	236 (48.8)	164 (47.4)	72 (52.2)	0.34
	\$48,000+	248 (51.2)	182 (52.6)	66 (47.8)	
	Missing	2	1	1	
Area	Metro	403 (85.2)	291 (86.6)	112 (81.8)	0.30
	Rural	11 (2.3)	6 (1.8)	5 (3.6)	
	Urban	59 (12.5)	39 (11.6)	20 (14.6)	
	Missing	13	11	2	
Distance to hospital	<50 miles	402 (83.2)	289 (83.8)	113 (81.9)	0.62
	50+ miles	81 (16.8)	56 (16.2)	25 (18.1)	
	Missing	3	2	1	
Charlson-Deyo Score	0-1	435 (89.5)	308 (88.8)	127 (91.4)	0.40
	2-3	51 (10.5)	39 (11.2)	12 (8.6)	
Grade	Well differentiated	119 (27.2)	92 (28.6)	27 (23.3)	0.07
	Moderately differentiated	213 (48.6)	161 (50)	52 (44.8)	
	Poorly or Undifferentiated	106 (24.2)	69 (21.4)	37 (31.9)	
	Missing	48	25	23	
NCDB Analytic Stage Group	Stage I	188 (38.7)	137 (39.5)	51 (36.7)	0.63
	Stage II	162 (33.3)	114 (32.9)	48 (34.5)	
	Stage III	71 (14.6)	47 (13.5)	24 (17.3)	
	Stage IV	65 (13.4)	49 (14.1)	16 (11.5)	
	Missing	48	25	23	
Involvement of Corpus Spongiosum/Cavernosum	No	239 (58.4)	180 (60.8)	59 (52.2)	0.11
	Yes	170 (41.6)	116 (39.2)	54 (47.8)	
	Missing	77	51	26	
Regional Lymph Node Surgery	No	344 (71.1)	249 (72)	95 (68.8)	0.49
	Yes	140 (28.9)	97 (28)	43 (31.2)	
	Missing	2	1	1	
Surgery	None or Tumor Destruction	37 (7.6)	23 (6.6)	14 (10.1)	0.38
	Excisional Biopsy	125 (25.7)	88 (25.4)	37 (26.6)	
	Surgery	324 (66.7)	236 (68)	88 (63.3)	
Surgical Margins	Negative	376 (87)	273 (86.7)	103 (88)	0.71
	Positive	56 (13)	42 (13.3)	14 (12)	
	Missing	54	32	22	
	Missing	54	32	22	
Radiation	No	432 (88.9)	310 (89.3)	122 (87.8)	0.62
	Yes	54 (11.1)	37 (10.7)	17 (12.2)	
Chemotherapy	No	389 (80)	274 (79)	115 (82.7)	0.35
	Yes	97 (20)	73 (21)	24 (17.3)	

- Included are 486 patients with penile squamous cell cancer, of which 139 (29%) were HPV positive, and 347 (71%) were HPV negative.
- Greater than 50% of patients who tested HPV +ve were < 65 years old, Caucasian, lived in low-income areas (< \$48,000), and had public insurance or no insurance. Similar incidence patterns were noted in HPV -ve patients.
- About 77% pts who were HPV +ve had a moderate to poorly differentiated tumor. Most HPV +ve presented with early-stage cancer, and about 12% were stage IV at diagnosis.

MULTIVARIABLE ANALYSIS

Variables	Hazard Ratio	Estimates		
		HR	95% CI	p
Age				<.01
65+ vs <65	1.95	(1.41-2.71)		
Charlson-Deyo Score				0.04
2-3 vs 0-1	1.67	(1.02-2.73)		
Stage				<.01
I vs IV	0.12	(0.07-0.20)		
II vs IV	0.16	(0.10-0.28)		
III vs IV	0.20	(0.12-0.36)		
HPV				0.04
Negative vs Positive	1.49	(1.02-2.18)		
Surgery				0.77
Yes vs No	1.06	(0.70-1.62)		
Radiation				0.78
Yes vs No	1.08	(0.61-1.92)		
Chemotherapy				0.98
Yes vs No	0.99	(0.57-1.74)		

OVERALL SURVIVAL



- Multivariable analysis (MVA) shows superior survival among patients with age <65 years, low comorbidity score (0-1), and earlier stage at diagnosis.
- 5-year overall survival (OS) was better among HPV +ve 62% vs. 50% in HPV -ve patients.
- Patients with HPV +ve adjusted for age, comorbidities, stage, and treatment showed significantly improved survival.
- HPV -ve patients had 1.49 times increased risk of death compared to HPV +ve.

Conclusions

- HPV positive penile cancer is associated with significantly improved survival independent of age, comorbidities, stage, and treatment modality.
- This study reiterates the prognostic significance of HPV status and testing for HPV status at diagnosis should be a standard practice