The influence of racial disparity on oncologic outcomes for patients with penile cancer: a SEER population-based study

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Abstract

Purpose: Penile cancer (PC) is an uncommon malignancy in the urinary system of males. The present study aims to compare survival outcomes of PC patients among racial/ethnic groups in the United States.

Methods and materials: Patients with PC were identified in the Surveillance, Epidemiology, and End Results (SEER) registries from 2004 to 2015. The SEER database represents 28% of the U.S. population. Race/ethnicity was categorized as non-hispanic white (NHW), hispanic white (HW), black, Asian/Pacific Islander (A/PI), or American Indian/Alaskan native (AI/AN). Kaplan-Meier method with the log-rank test was used to assess cancer-specific survival (CSS) and overall survival (OS). Multivariate analysis was conducted using Cox's proportional hazard model.

Results: A total of 3955 patients with PC were included. There were significant differences in age, marital status, tumor location, histology, grade, lymphadenectomy, and radiotherapy according to race/ethnicity. Univariate analysis revealed that A/PIs were significantly associated with better CSS ($p=0.005$) and OS ($p=0.025$) for most subtypes. The 5-year CSS rates for NHWs, HWs, blacks, A/PIs and AI/ANs were 79.4%, 74.2%, 75.9%, 87.1%, and 78.9%, respectively. The 5-year OS rates for NHWs, HWs, blacks, A/PIs and AI/ANs were 63.4%, 64.1%, 60.5%, 73.0%, and 70.9%, respectively. After adjusting for other factors, racial disparity was an independent risk factor for CSS and OS in the multivariate analysis ($p=0.010$ and $p=0.017$, respectively).

Conclusions: Our results suggested that racial differences existed among PC patients in the United States with respect to patient clinicopathological features and survival. Long-term survival disparities were evident in PC patients, that the survival of NHWs, HWs, and blacks was worse than that of A/PIs.

1. Introduction

Penile cancer (PC) is a rare malignancy, accounting for approximately 2–4 cases per 100,000 men in the developing countries of Africa, Asia and South America; however, it is significantly rarer in the United States and Europe (0.3-1 cases per 100,000 males) [1].

In the United States, the incidence of PC is affected by race/ethnicity, with the highest incidence in hispanic whites (HWs) (1.01/100,000), followed by American Indian/Alaskan natives (AI/ANs) (0.77/100,000), African Americans (0.62/100,000) and non-hispanic whites (NHWs) (0.51/100,000)[2]. Five-year cancer-specific survival (CSS) rate for PC varied from almost 90% in Stage I to almost 0% in Stage IV[3]. Studies showed that pathological subtype, perineural invasion, lymphovascular invasion[4, 5], depth of invasion and grade in the primary tumor were strong predictors of poor prognosis and high cancer-specific mortality[6]. So far, few studies had explored race/ethnicity as a prognostic factor in PC survival.

However, increasing evidences suggested that race/ethnicity was a poor prognostic indicator in various types of malignancies, including bladder cancer, testicular cancer, T-cell lymphoma and ovarian cancer[7–10]. Because of the low incidence of penile cancer, no randomized studies had been completed to compare survival outcomes according to race/ethnicity. Using the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program registry, the present study aimed to evaluate the influence of race and ethnicity on the oncological outcomes of penile cancer.

2. Materials And Methods

2.1. Data source and study population

Data were retrieved from 18 SEER cancer registries in the United States describing all PC patients diagnosed between 2004 and 2015 (n = 3,999). Patients were identified using the International Classification of Diseases for Oncology (ICD-O) topography code of C60.0-60.9, and those registered between 2004 and 2015 were selected. Forty four patients with unknown race/ethnicity were excluded from the primary statistical analyses. Therefore, the clinicopathological data of the remaining 3955 patients were retrospectively analyzed.

2.2. Variables definition

Demographic characteristics of patients included age at diagnosis, marital status and race/ethnicity. Tumor characteristics of patients included tumor location, histology, TNM status, stage, grade, lymphovascular invasion (LVI), and lymphadenectomy. Treatment information included surgery, radiotherapy, and chemotherapy. Marital status was defined as married, unmarried or unknown. Unmarried included never married, separated/divorced, and widowed patients. Race/ethnicity was categorized as NHW, HW, black, Asian/Pacific Islander (A/PI), and AI/AN. Tumor location was defined as primary tumor originated in glans penis, body of penis, prepuce, overlapping lesion of penis, and penis not otherwise specified. The most common histology of PC was squamous cell carcinoma, so other rare histology types were all set as other types. TNM status were assessed according to the American Joint Committee on Cancer (AJCC), sixth edition. And tumor grade was assigned according to the SEER database as grades I, II, III, IV, and unknown. Surgery was categorized as no surgery, non-radical surgery, and radical surgery.

2.3. Statistical Analyses

SPSS version 23.0 (IBM Corp, Armonk, NY) was used for all statistical analyses. Chi-square test was used to determine the significance of differences between categorical variables stratified by race/ethnicity. The Kaplan-Meier method with the log-rank test was used to assess CSS and OS. Cox's proportional hazard model was used to estimate hazard ratios (HRs) and 95% CIs of death from PC or any cause, comparing each race/ethnicity to A/PIs. All reported p-values were two-tailed and a $p < 0.050$ was considered significant.

3. Results

3.1. Clinicoathological Features

The clinicopathological characteristics of 3955 patients are listed in Table 1. There were 2567 NHW (64.9%), 767 HW (19.4%), 401 black (10.1%), 178 A/PI (4.5%), and 42 AI/AN (1.1%) patients diagnosed as PC. There were significant differences in age, marital status, tumor location, histology, grade, lymphadenectomy, and radiotherapy according to race/ethnicity (all $p < 0.050$). HWs tended to have a younger age at diagnosis than other race/ethnicity. AI/ANs were more likely to have higher grades (G II+III more than 64%). Although statistical significance existed between different races, the most common primary tumor location and histology were glans penis and squamous cell carcinoma, respectively. And more than 75% and 83% of the PC patients had not received lymphadenectomy and radiotherapy, respectively. There were no significant differences in surgery approaches, pathological TNM stages, LVI, or chemotherapy according to race/ethnicity (all $p > 0.050$).

3.2. Oncologic Outcomes

Follow-up information was available for 3955 PC patients with known race/ethnicity, and 1365 deaths (34.5%) occurred over a median follow-up time of 33 months (interquartile range, 13 to 72 months). Overall, 713 patients (18.0%) in the dataset died specifically of PC. Survival curves showed significant variation by race/ethnicity; median survival time of PC patients was 35, 29, 29, 42.5, and 42.5 months for NHWs, HWs, blacks, A/PIs, and AI/ANs, respectively. The 5-year CSS rates for NHWs, HWs, blacks, A/PIs and AI/ANs were 79.4%, 74.2%, 75.9%, 87.1%, and 78.9%, respectively (Figure 1A). The 5-year OS rates for NHWs, HWs, blacks, A/PIs and AI/ANs were 63.4%, 64.1%, 60.5%, 73.0%, and 70.9%, respectively (Figure 1B).

In the univariate analysis for cancer-specific mortality (Table 2), age, marital status, race/ethnicity, tumor location, surgery, pathological TNM stages, grade, LVI, lymphadenectomy, radiotherapy and chemotherapy were all associated with cancer-specific mortality. After adjusting for other factors, race/ethnicity ($p = 0.010$) was an independent risk factor for cancer-specific mortality in the multivariate analysis. In the univariate analysis for other-cause mortality (Table 3), age, marital status, race/ethnicity, surgery, pathological TNM stages, grade, LVI, lymphadenectomy, radiotherapy and chemotherapy were all associated with other-cause mortality. After adjusting for other factors, race/ethnicity ($p = 0.017$) was also an independent risk factor for other-cause mortality in the multivariate analysis. Compared with A/PIs, NHWs, HWs, and blacks had shorter survival (HR: 1.429; 95% CI: 1.069 to 1.909; HR: 1.570; 95% CI: 0.601 to 0.953; HR: 1.698; 95% CI: 1.225 to 2.355, respectively, Table 3).

4. Discussion

Although PC is a rare malignancy among men across the globe, it is a significant health problem in most of the developing countries. Because of rarity, there is a paucity of data to help with clinical decision making regarding the treatment of PC. To the best of our knowledge, whether there are racial differences in PC survival has not been fully explored and the present study is the first large study including 3955 PC patients. In this study, we found that there is a racial difference in the survival of PC patients, where NHWs, HWs, and blacks with PC showed a lower survival probability than A/PI patients.

Data from previous studies showed that there were different incidences regarding racial distribution. In developed countries, an overall incidence was around 1/100,000 males in Europe and the USA[11, 12]. In contrast, the incidence was much higher in South America, South East Asia and parts of Africa and could account for 1–2% of malignancies in men[2]. The annual age-adjusted incidence was 0.7-3.0/100,000 in India, 8.3/100,000 in Brazil and even higher in Uganda, where it was the most commonly diagnosed male cancer[2, 13]. More detailed in the USA, white Hispanics (1.01/100,000) had the highest incidence, followed by Alaskans and Native American Indians (0.77/100,000), African Americans (0.62/100,000) and white non-Hispanics (0.51/100,000). Consistent with other studies[14, 15], the present study showed that penile cancer was most commonly found in subjects of white ethnicity (including NWH and HW), accounting for 3334 (84.3%) of the cases, but it also occurred in 401 Blacks (10.1%), 178 Asians/Pacific Islanders (4.5%), and 42 American Indian/Alaskan Natives (1.1%).

Jonathan and his colleagues had reported that compared with whites, African-American men presented with a statistically significant decreased cancer-specific survival[15], but African-American patients had a higher stage of disease which may contribute some biases to their result. In our study, there were no significant differences in terms of TNM stages according to the race/ethnicity (Table 1). And after accounting for other factors, race/ethnicity was an independent risk factor for cancer-specific mortality and other-cause mortality in the multivariate analysis (Table 2 and Table 3).

However, the reasons behind these survival differences are poorly understood. Based on the theories from some other studies[16–19] on demonstrating the ethnic differences in chronic nephritis, myeloma and breast cancer, we suspect that racial disparity in the survival of patients with penile cancer may be due to the combined effects of biology and epidemiology. Potentially relevant biologic differences between races include genetic variations in pharmacokinetics or pharmacodynamics of therapeutic agents and genomic variations of the tumors. Disparities in health care delivery and socioeconomic status might delay the time of the diagnosis, and consequently, contribute to the delay of treatment, high rate of relapse, and death. Clearly, future studies in the United States would benefit from including detailed information on treatment and socioeconomic factors to better understand racial disparities in survival.

Our study has some limitations. First, this is a retrospective study. Second, the databases used in this study did not provide information on the main risk factors[20], such as lack of proper hygiene, phimosis, uncircumcision and HPV infection, which could act as confounding factors. Nonetheless the current study is still one of the largest cohorts of PC patient data from the population-based SEER cancer registries that cover approximately 28% of the US.

5. Conclusions

In conclusion, NHWs, HWs, and blacks diagnosed as PC had significantly worse survival outcomes, compared with A/PIs. More closed follow-up surveillance after treatment is needed for NHW, HW, and black patients with PC.

Abbreviations

PC, penile cancer; SEER, Surveillance, Epidemiology, and End Results; CSS, cancer-specific survival; OS, overall survival; AJCC, American Joint Committee on Cancer; ICD-O, International Classification of Diseases for Oncology); TNM, tumor, node and metastasis; HR, hazard ratio.

Declarations

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Availability of data and materials

The raw data underlying this paper is available upon request to from the corresponding author.

Authors' contributions

Xiaohong Su: Data collection/management, data analysis, manuscript writing/editing. Kaihui Wu and Shuo wang: Data collection/management, data analysis. Bingkun Li and Chuanyin Li: Data collection/management, manuscript editing. Xiangming Mao: Protocol/project development, revision of the manuscript and supervision. All authors have read and approve of the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics and consent to participate

The institutional review board approval was not required for the SEER program of the National Cancer Institute as it utilizes the public-use database.

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Tables

Table1. Clinical and pathological characteristics of 3955 patients with penile cancer stratified by Race and Ethnicity, from SEER Cancer Registries, 2004 to 2015

Characteristic	Race/ethnicity					Chi-square	p value
	NHW (n=2567) 70(61-79)	HW (n=767) 60(48-74)	Black (n=401) 65(54-75)	A/PI (n=178) 69(58-78)	AI/AN (n=42) 68(60-74)		
Age, median (IQR)						124.470	<0.001*
Marital status						69.608	<0.001*
Married	1444(56.3)	429(55.9)	166(41.4)	118(55.1)	24(57.1)		
Unmarried	891(34.7)	284(37.0)	213(53.1)	44(24.7)	11(26.2)		
Unknown	232(9.0)	54(7.0)	22(5.5)	16(9.0)	7(16.7)		
Histology						11.567	0.021*
Squamous cell carcinoma	2175(84.7)	659(85.9)	346(86.3)	136(76.4)	34(81.0)		
Other types	392(15.3)	108(14.1)	55(13.7)	42(23.6)	8(19.0)		
Surgery						8.090	0.425
No	291(11.3)	65(8.5)	48(12.0)	15(8.4)	6(14.3)		
Non-radical surgery	2200(85.7)	21(2.7)	12(3.0)	6(3.4)	2(4.8)		
Radical surgery	76(3.0)	681(88.8)	341(85.0)	157(88.2)	34(81.0)		
Pathological T stage						23.486	0.101
T0-Ta-T1	1474(57.4)	399(52.0)	230(57.4)	103(57.9)	23(54.8)		
T2	509(19.8)	191(24.9)	67(16.7)	29(16.3)	9(21.4)		
T3	341(13.3)	111(14.5)	62(15.5)	26(14.6)	5(11.9)		
T4	63(2.5)	17(2.2)	15(3.7)	6(3.4)	0(0.0)		
Tx	180(7.0)	49(6.4)	27(6.7)	14(7.9)	5(11.9)		
Pathological N stage						22.260	0.135
N0	1948(75.9)	536(69.9)	296(73.8)	129(72.5)	30(71.4)		
N1	156(6.1)	49(6.4)	24(6.0)	11(6.2)	5(11.9)		
N2	141(5.5)	67(8.7)	27(6.7)	13(7.3)	4(9.5)		
N3	108(4.2)	43(5.6)	20(5.0)	6(3.4)	1(2.4)		
Nx-NA	214(8.3)	72(9.4)	34(8.5)	19(10.7)	2(4.8)		
Pathological M stage						7.478	0.486
M0	2321(90.4)	689(89.8)	357(89.0)	157(88.2)	36(85.7)		
M1	79(3.1)	31(4.0)	21(5.2)	7(3.9)	2(4.8)		
Mx/NA	167(6.5)	47(6.1)	23(5.7)	14(7.9)	4(9.6)		
Stage						24.612	0.077
I	1303(50.8)	333(43.4)	205(51.1)	87(48.9)	21(50.0)		
II	459(17.9)	151(19.7)	57(14.2)	27(15.2)	9(21.4)		
III	357(13.9)	131(17.1)	58(14.5)	28(15.7)	5(11.9)		
IV	206(8.0)	70(9.1)	46(11.5)	14(7.9)	3(7.1)		
Unknown	242(9.4)	82(10.7)	35(8.7)	22(12.4)	4(9.5)		
Grade						57.156	<0.001*
GI	551(21.5)	229(29.9)	74(18.5)	49(27.5)	5(11.9)		
GII	929(36.2)	296(38.6)	151(37.7)	59(33.1)	15(35.7)		
GIII	467(18.2)	122(15.9)	84(20.9)	27(15.2)	12(28.6)		
GIV	24(0.9)	3(0.4)	6(1.5)	1(0.6)	0(0.0)		

Unknown	596(23.2)	117(15.3)	86(21.4)	42(23.6)	10(23.8)		
LVI						5.887	0.660
No	664(25.9)	227(29.6)	111(27.7)	50(28.1)	11(26.2)		
Yes	189(7.4)	60(7.8)	26(6.5)	12(6.7)	4(9.5)		
Unknown	1714(66.8)	480(62.6)	264(65.8)	116(65.2)	27(64.3)		
Lymphadenectomy						20.652	0.008*
No	2098(81.7)	577(75.2)	320(79.8)	143(80.3)	36(85.7)		
Yes	419(16.3)	174(22.7)	70(17.5)	29(16.3)	6(14.3)		
Unknown	50(1.9)	16(2.1)	11(2.7)	6(3.4)	0(0.0)		
Radiotherapy						14.136	0.007*
No	2405(93.7)	705(91.9)	372(92.8)	173(97.2)	35(83.3)		
Yes	162(6.3)	62(8.1)	29(7.2)	5(2.8)	7(16.7)		
Chemotherapy						8.990	0.061
No	2339(91.1)	674(87.9)	359(89.5)	156(87.6)	39(92.9)		
Yes	228(8.9)	93(12.1)	42(10.5)	22(12.4)	3(7.1)		

Abbreviation: NHW, Non-Hispanic White; HW, Hispanic White; A/PI, Asian/Pacific Islander; AI/AN, American Indian/Alaskan Native; IQR, interquartile range; NOS, not otherwise specified; NA, not available; LVI, lymphovascular invasion

* statistically significant.

Table 2 Univariate and multivariate regression analyses for CSS

Characteristic	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age	1.008	1.003-1.014	0.004 [*]	1.014	1.008-1.020	<0.001 [*]
Marital status						
Married	Ref.		<0.001 [*]	Ref.		<0.001 [*]
Unmarried	1.472	1.266-1.712	<0.001 [*]	1.304	1.118-1.520	0.001 [*]
Unknown	0.621	0.437-0.883	0.008 [*]	0.560	0.389-0.806	0.002 [*]
Race/ethnicity						
A/PI	Ref.		0.005 [*]	Ref.		0.010 [*]
NHW	1.697	1.084-2.656	0.021 [*]	1.743	1.111-2.736	0.016 [*]
HW	2.052	1.288-3.271	0.003 [*]	2.168	1.355-3.469	0.001 [*]
Black	2.191	1.345-3.657	0.002 [*]	2.051	1.252-3.358	0.004 [*]
AI/AN	1.417	0.569-3.529	0.454	1.579	0.631-3.952	0.329
Histology						
Squamous cell carcinoma	Ref.		0.482			
Other types	0.927	0.750-1.145				
Surgery						
Non-radical surgery	Ref.		<0.001 [*]	Ref.		<0.001 [*]
Radical surgery	3.086	2.553-3.731	<0.001 [*]	1.790	1.432-2.238	<0.001 [*]
No surgery	2.264	1.615-3.172	<0.001 [*]	1.185	0.837-1.679	0.339
Pathological T stage						
T0-Ta-T1	Ref.		<0.001 [*]	Ref.		0.006 [*]
T2	2.095	1.723-2.546	<0.001 [*]	1.139	0.845-1.535	0.393
T3	3.042	2.487-3.720	<0.001 [*]	1.222	0.897-1.667	0.204
T4	6.173	4.505-8.458	<0.001 [*]	1.651	1.059-2.574	0.027 [*]
Tx	4.811	3.793-6.102	<0.001 [*]	1.925	1.339-2.768	<0.001 [*]
Pathological N stage						
N0	Ref.		<0.001 [*]	Ref.		<0.001 [*]
N1	3.939	3.100-5.004	<0.001 [*]	2.792	2.083-3.742	<0.001 [*]
N2	5.453	4.388-6.776	<0.001 [*]	3.169	2.306-4.356	<0.001 [*]
N3	8.583	6.832-10.784	<0.001 [*]	2.968	1.990-4.428	<0.001 [*]
Nx-NA	3.630	2.894-4.551	<0.001 [*]	2.453	1.580-3.806	<0.001 [*]
Pathological M stage						
M0	Ref.		<0.001 [*]	Ref.		0.002 [*]
M1	9.320	7.382-11.767	<0.001 [*]	1.793	1.244-2.583	0.002 [*]
Mx/NA	2.537	1.996-3.226	<0.001 [*]	1.528	0.982-2.379	0.060
Stage						
I	Ref.		<0.001 [*]	Ref.		<0.001 [*]
II	2.244	1.773-2.839	<0.001 [*]	1.470	1.009-2.143	0.045 [*]
III	3.820	3.065-4.760	<0.001 [*]	1.748	1.168-2.615	0.007 [*]
IV	11.745	9.476-14.557	<0.001 [*]	2.618	1.562-4.388	<0.001 [*]
Unknown	4.007	3.114-5.157	<0.001 [*]	0.701	0.403-1.220	0.209
Grade						
G I	Ref.		<0.001 [*]	Ref.		<0.001 [*]
G II	2.432	1.910-3.096	<0.001 [*]	1.731	1.350-2.220	<0.001 [*]
G III	3.590	2.775-4.644	<0.001 [*]	1.813	1.379-2.382	<0.001 [*]

G IV	4.628	2.403-8.914	<0.001 [*]	1.998	1.016-3.929	0.045 [*]
Unknown	1.992	1.522-2.606	<0.001 [*]	1.172	0.880-1.560	0.278
LVI						
No	Ref.		<0.001 [*]	Ref.		0.494
Yes	2.121	1.597-2.816	<0.001 [*]	0.970	0.720-1.307	0.842
Unknown	1.269	1.052-1.531	0.013 [*]	1.098	0.903-1.336	0.348
Lymphadenectomy						
No	Ref.		<0.001 [*]	Ref.		<0.001 [*]
Yes	1.519	1.279-1.804	<0.001 [*]	0.666	0.540-0.821	<0.001 [*]
Unknown	3.797	2.669-5.401	<0.001 [*]	2.267	1.492-3.446	<0.001 [*]
Radiotherapy						
No	Ref.		<0.001 [*]	Ref.		0.705
Yes	2.442	1.967-3.031		1.047	0.824-1.330	
Chemotherapy						
No	Ref.		<0.001 [*]	Ref.		0.741
Yes	3.213	2.693-3.834		1.037	0.835-1.289	

Abbreviation: CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval; Ref., reference; NHW, Non-Hispanic White; HW, Hispanic White; A/PI, Asian/Pacific Islander; AI/AN, American Indian/Alaskan Native; NOS, not otherwise specified; NA, not available; LVI, lymphovascular invasion

^{*} statistically significant.

Table 2 Univariate and multivariate regression analyses for OS

Characteristic	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age	1.030	1.026-1.035	<0.001 [*]	1.033	1.029-1.038	<0.001 [*]
Marital status						
Married	Ref.		<0.001 [*]	Ref.		<0.001 [*]
Unmarried	1.452	1.300-1.621	<0.001 [*]	1.345	1.203-1.504	<0.001 [*]
Unknown	0.854	0.684-1.066	0.164	0.757	0.601-0.953	0.018 [*]
Race/ethnicity						
A/PI	Ref.		0.027 [*]	Ref.		0.017 [*]
NHW	1.462	1.097-1.949	0.010 [*]	1.429	1.069-1.909	0.016 [*]
HW	1.370	1.007-1.864	0.045 [*]	1.570	0.601-0.953	0.018 [*]
Black	1.664	1.205-2.298	0.002 [*]	1.698	1.225-2.355	0.002 [*]
AI/AN	1.163	0.618-2.186	0.640	1.237	0.656-2.333	0.511
Histology						
Squamous cell carcinoma	Ref.		0.091			
Other types	0.874	0.748-1.022				
Surgery						
Non-radical surgery	Ref.		<0.001 [*]	Ref.		<0.001 [*]
Radical surgery	2.280	1.955-2.659	<0.001 [*]	1.501	1.260-1.787	<0.001 [*]
No surgery	1.657	1.258-2.183	<0.001 [*]	1.175	0.886-1.558	0.263
Pathological T stage						
T0-Ta-T1	Ref.		<0.001 [*]	Ref.		0.017 [*]
T2	1.537	1.340-1.763	<0.001 [*]	1.074	0.833-1.384	0.584
T3	1.967	1.695-2.282	<0.001 [*]	1.231	0.940-1.612	0.131
T4	3.127	2.378-4.111	<0.001 [*]	1.403	0.937-2.100	0.100
Tx	2.854	2.369-3.438	<0.001 [*]	1.613	1.204-2.161	0.001 [*]
Pathological N stage						
N0	Ref.		<0.001 [*]	Ref.		<0.001 [*]
N1	2.092	1.718-2.546	<0.001 [*]	1.965	1.554-2.484	<0.001 [*]
N2	2.737	2.281-3.284	<0.001 [*]	2.384	1.835-3.096	<0.001 [*]
N3	4.030	3.302-4.919	<0.001 [*]	2.403	1.681-3.434	<0.001 [*]
Nx-NA	2.212	1.864-2.625	<0.001 [*]	1.725	1.219-2.442	0.002 [*]
Pathological M stage						
M0	Ref.		<0.001 [*]	Ref.		<0.001 [*]
M1	5.733	4.628-7.101	<0.001 [*]	1.887	1.338-2.660	<0.001 [*]
Mx/NA	1.961	1.626-2.365	<0.001 [*]	1.369	0.971-1.931	0.073
Stage						
I	Ref.		<0.001 [*]	Ref.		0.004 [*]
II	1.522	1.306-1.773	<0.001 [*]	1.312	0.981-1.754	0.067
III	2.063	1.771-2.403	<0.001 [*]	1.372	0.998-1.886	0.051
IV	4.824	4.096-5.682	<0.001 [*]	1.880	1.208-2.927	0.005 [*]
Unknown	2.249	1.884-2.683	<0.001 [*]	0.737	0.486-1.116	0.149
Grade						
G I	Ref.		<0.001 [*]	Ref.		<0.001 [*]
G II	1.529	1.315-1.777	<0.001 [*]	1.293	1.107-1.510	0.001 [*]
G III	2.164	1.831-2.557	<0.001 [*]	1.359	1.137-1.625	0.001 [*]
G IV	2.193	1.255-3.830	0.006 [*]	1.266	0.718-2.233	0.415

Unknown	1.290	1.087-1.532	0.004*	0.963	0.803-1.155	0.682
LVI						
No	Ref.		<0.001*	Ref.		0.160
Yes	1.991	1.599-2.479	<0.001*	1.251	0.995-1.573	0.056
Unknown	1.215	1.056-1.399	0.007*	1.073	0.928-1.239	0.341
Lymphadenectomy						
No	Ref.		<0.001*	Ref.		<0.001*
Yes	1.045	0.911-1.199	0.531	0.694	0.588-0.821	<0.001*
Unknown	2.719	2.047-3.611	<0.001*	1.816	1.299-2.539	<0.001*
Radiotherapy						
No	Ref.		<0.001*	Ref.		0.907
Yes	1.696	1.413-2.037		1.012	0.827-1.238	
Chemotherapy						
No	Ref.		<0.001*	Ref.		0.810
Yes	1.942	1.666-2.265		1.023	0.848-1.235	

Abbreviation: OS, overall survival; HR, hazard ratio; CI, confidence interval; Ref., reference; NHW, Non-Hispanic White; HW, Hispanic White; A/PI, Asian/Pacific Islander; AI/AN, American Indian/Alaskan Native; NOS, not otherwise specified; NA, not available; LVI, lymphovascular invasion

* statistically significant.

Figures

Figure 1

Influence of the Race and Ethnicity on Cancer-Specific Survival (A) and Overall Survival (B) in Penile Cancer patients.