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ORIGINAL PAPER

A population-based analysis of the effect of marital status on overall and cancer-specific mortality in patients with squamous cell carcinoma of the penis

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Abstract
Purpose The association between marital status and tumor stage and grade, as well as overall mortality (OM) and cancer-specific mortality (CSM) received little attention in patients with squamous cell carcinoma of the penis (SCCP).
Methods We relied on the surveillance, epidemiology, and end results (SEER) 17 database to identify patients diagnosed with primary SCCP. Logistic and Cox regression models, respectively, addressed the effect of marital status on the rate of locally advanced disease and its effect on OM and CSM. Covariates consisted of age, race, socioeconomic status, year of surgery, and SEER registries.
Results Between 1988 and 2006, 1,884 patients with SCCP were identified. At surgery, 1,192 (63.3 %) were married and 966 (51.3 %) had locally advanced disease. In multivariable logistic regression models predicting locally advanced disease at surgery, unmarried men had a 1.5-fold higher ($p < 0.001$) risk than others. In multivariable Cox models predicting CSM, marital status had no effect [hazard ratio (HR) = 1.3, $p = 0.1$]. Finally, in multivariable Cox models predicting OM, unmarried men had a 1.3-fold higher ($p = 0.001$) risk than others.
Conclusion Unmarried men tend to present with less favorable disease stage at SCCP. Moreover, unmarried men tend to live less long than their married counterparts. However, marital status has no effect on CSM.

Keywords Penile carcinoma · Marital status · Surveillance, epidemiology, and end results (SEER) program

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Introduction

In a variety of malignancies, the effect of marital status is being increasingly recognized as a determinant of stage and grade at presentation, as well as a determinant of the evolution of treated cancer. For example, in breast cancer and in melanoma, favorable sociodemographic factors, including married individuals, are associated with better survival [1, 2]. Similarly, several investigators demonstrated the protective effect of marital status in several other solid tumors. In general, married individuals present with less advanced stage at diagnosis. This applies to cervical, lung, or breast cancers [3–5]. Moreover, married individuals have lower mortality rates. This applies to malignant melanoma, as well as colorectal, oral, gastric, bladder, or prostate cancers [6–12]. Additionally, married men tend to obtain better care than their unmarried counterparts [13].

Despite the beneficial effects related to married status in several solid tumors, the effect of marital status was only examined by several investigators in squamous cell carcinoma of the penis (SCCP) [14–16]. Of those studies, two relied on historic populations (years 1935–973) in the context of SCCP ($n = 64$–120). The most recent report relied on 1,394 individuals treated between 1973 and 1998, of whom 84 % were married [14]. This report suggested a beneficial effect on stage at presentation and confirmed a higher disease-specific survival for married men diagnosed with localized or regional stages at presentation ($p \leq 0.001$). Despite its large sample size, it is possible that the relationship between marital status and stage at presentation, as well as mortality, changed in more recent years. This change may be related to possible increases or decreases in the proportion of married and unmarried individuals. Similarly, it is possible that changes in the dynamics of marriage and their effect on cancer may have occurred over time. Therefore, the benefits of marriage may not have an equally strong effect in more contemporary years, as it was reported from 1973 to 1998 [14].

Based on these considerations, we set to examine the effect of marital status on stage and grade at presentation, as well as on mortality in a contemporary cohort of patients with SCCP. Our hypothesis stated that married patients may fare better than their unmarried counterparts.

Materials and methods

Study population

Within 17 surveillance, epidemiology, and end results (SEER) tumor registries, we identified all men treated for primary SCCP between 1988 and 2006 who underwent primary tumor excision (PTE) (excisional biopsy, partial or total penectomy) according to two diagnostic codes: the tenth revision of the International Classification of Disease for Oncology second edition (ICD-O-2) [C60.0–60.9] and the ICD-O-3 codes for histological subtype (squamous cell carcinoma type; ICD-O-3: 8070–8076). The SEER database of the National Cancer Institute (NCI) program covers approximately 26 % of the US population and is considered representative of the United States with regard to demographic composition, as well as of cancer incidence and mortality [17]. Registries include the Alaska Natives, Metropolitan Atlanta, Greater California, Los Angeles, San Francisco-Oakland, San Jose-Monterey, as well as Connecticut, New Jersey, Detroit (Metropolitan), Iowa, Kentucky, Utah, Louisiana, New Mexico, Rural Georgia, Seattle (Puget Sound), and Hawaii.

We relied on the SEER primary tumor stage to stratify patients between T1, T2, T3, and T4 stage groupings [18]. Only patients with squamous cell histology were included. Exclusions consisted of unknown tumor stage ($n = 372$), unknown tumor grade ($n = 324$), and unknown marital status ($n = 102$) according to the SEER code. Finally, patients treated in, respectively, Alaska ($n = 4$) and Rural Georgia ($n = 3$) SEER registries were excluded from all analyses due to exceedingly low numbers of observations in these two regions. These criteria resulted in 1,884 assessable patients that represent the focus of this study.

For all patients, the following variables were analyzed: tumor stage and grade, marital status, year of PTE, age, race, socioeconomic status (SES), and SEER registry. For each patient, SES variables included median family income within the zip code of residence, as well as county level of poverty and education. The level of poverty was defined as the percentage of individuals living below the poverty line within the patient's county of residence. Education level was defined as the percentage of individuals without a high school diploma within the patient's county of residence. These percentages were defined according to the United States Census Bureau tables [19, 20]. Based on previously used methodology, those three variables were converted into normal scores. The latter were summed to create a composite variable [21, 22]. The composite variable was then stratified according to the median. Low values were indicative of low and high values of high SES, respectively [21, 22].

Statistical analyses

The χ^2 test was used to compare the statistical significance of the differences in proportions. The t test was used to compare the statistical significance of means' differences.

The first part of the analyses focused on the effect of marital status on stage and grade at PTE. Univariable and multivariable logistic regression models tested the

statistical significance and the independent predictor status of risk factors that may predispose to locally advanced stage (T3-4/N1-3/M1) or high grade (III or IV) (LASG) at PTE. For marital status, we stratified our cohort according to married versus unmarried men (single, widowed, divorced, or separated) in accordance with previous methodology [23, 24]. Candidate risk factors consisted of patient's marital status (married vs. unmarried), age at PTE categorized into quartiles (≤58 vs. 59–68 vs. 69–78 vs. ≥79 years), race (white vs. black vs. other), SEER registries, year of PTE quartiles (1988–1996 vs. 1997–2001 vs. 2002–2003 vs. 2004–2006), and year of SES (low vs. high SES).

The second part of the analyses focused on the effect of marital status on overall mortality (OM) and on CSM. We relied on Kaplan–Meier plots to graphically illustrate survival rates according to marital status. OM and CSM rates were then calculated using life tables. Separate multivariable Cox regression analyses tested the effect of marital status, stage at presentation, grade, year of PTE, race, age, SES, and SEER registries on first CSM and then on OM. The date of PTE was considered as the starting time of observation, and non-cancer deaths were treated as censored elements.

All statistical analyses were performed using the Statistical Package for Social Science, version 15.0 (SPSS®, Chicago, IL) statistical software, and all tests were two-sided, with a significance level set at <0.05.

Results

Table 1 shows the descriptive characteristics of the entire cohort. The average age was 66.8 years (median 68.0). White race predominated (84.7 %). Most had LASG SCCP (51.3 %), and most patients were in the low SES category (52.0 %). Overall, 63.3 % were married. Between 1988 and 2006, the proportion of married individuals ranged from 66.7 to 63.8 % ($p = 0.5$).

After stratification according to marital status, several important differences were recorded (Table 1A). First, the rate of LASG was higher in unmarried than married men (57.1 vs. 47.9 %, $p = 0.001$). Statistically significant differences also distinguished unmarried from married men with respect to race. Specifically, African American men were more frequently unmarried than married (15.9 vs. 6.1 %, $p < 0.001$). Conversely, no statistically significant differences were recorded in SES ($p = 0.6$) or SEER registry ($p = 0.3$) between unmarried and married men. Interestingly, the rate of LASG decreased over time (Table 1B). For example, the LASG rate between 1988 and 1996 was 32.6 versus 29.6, 15.7, and 22.0 % for, respectively, 1997–2001, 2002–2003, and 2004–2006 periods (χ^2 trend, $p < 0.001$). No other statistically significance temporal trends were recorded.

Univariable logistic regression analyses demonstrated that unmarried individuals had a 1.4-fold higher risk of harboring LASG at PTE ($p < 0.001$) (Table 2). This risk remained statistically significant [odds ratio (OR) = 1.5, $p < 0.001$] after adjusting for all covariates (age, race, SES, SEER registries, and year of PTE). Interestingly, patients treated in more contemporary study years had more favorable stage and grade at PTE (χ^2 trend, $p = 0.01$). For example, relative to the first year of surgery quartile (1988–1996) and after adjusting for all other covariates, patients treated between 2004 and 2006 were 30 % less likely to harbor LASG at PTE ($p = 0.004$). Individuals treated between 2002–2003 and 1997–2001 were, respectively, 40 ($p = 0.003$) and 30 % ($p = 0.01$) less likely to harbor LASG. Similarly, multivariable analyses indicated that SEER registry may also exert an independent effect on LASG at PTE. For example, patients treated in Utah, Seattle, Iowa, Atlanta, or Detroit registries were, respectively, 4.2 ($p < 0.001$), 2.7 ($p < 0.001$), 2.7 ($p < 0.001$), 2.3 ($p = 0.008$), and 1.5 ($p = 0.04$) times more likely to have an LASG at PTE than their Greater California counterparts. Conversely, patients treated in the Louisiana SEER registry were 50 % less likely to have an LASG at PTE (OR = 0.5, $p = 0.005$) (Table 2).

The second part of our analyses focused on the effect of MS on OM and CSM. Kaplan–Meier curves illustrating CSM and OM in the overall population are shown in Figs. 1 and 2. The 5-year CSM and OM-free rates for the entire cohort were, respectively, 83.1 and 54.4 %. After stratification according to MS (Fig. 1), unmarried men were more likely to succumb to SCCP than married men, as evidenced by respective 5-year CSM-free rates of 79.1 and 85.2 % (log-rank test: $p = 0.003$). In OM analyses (Fig. 2), married men also showed better survival rates, as evidenced by 5-year OM-free rates of 59.1 vs. 46.2 % (log-rank test: $p < 0.001$).

We then relied on Cox regression models that tested and quantified the independent predictor status of marital status on CSM and OM. In CSM analyses (Table 3B), marital status failed to demonstrate independent predictor status [hazard ratio (HR) = 1.3, $p = 0.1$]. LASG at PTE increased the rate of CSM by 3.4-fold fashion ($p < 0.001$). Additionally, patients from New Mexico had a 2.2-fold higher rate of CSM ($p = 0.008$). Conversely, patients from Seattle (Puget Sound) had a 70 % decrease in the rate of CSM relative to Greater California ($p = 0.009$).

In OM analyses (Table 3A), multivariable models showed that unmarried men have a 1.3-fold higher rate of OM relative to their married counterparts (HR = 1.3, $p = 0.001$). LASG at PTE ($p < 0.001$) and age ($p < 0.001$) also represented independent predictors of OM. For example, patients with LASG at PTE had a 1.7-fold ($p < 0.001$) higher mortality rate than patients with

Table 1 Descriptive characteristics of patients with squamous cell carcinoma of the penis ($n = 1,884$) stratified according to marital status [A] and tumor stage and grade at presentation [B]

Variables	Overall ($n = 1,884$)	[A] Marital status			[B] Stage and grade at presentation		
		Married ($n = 1,192$)	Unmarried ($n = 692$)	p	Localized ($n = 918$)	Locally advanced ($n = 966$)	p
Marital status							<0.001
Married	1,192 (63.3)	–	–	–	621 (67.6)	571 (59.1)	
Unmarried	692 (36.7)				297 (32.4)	395 (40.9)	
Stage and grade at presentation				0.001			
Localized	918 (48.7)	621 (52.1)	297 (42.9)		–	–	–
Locally advanced	966 (51.3)	571 (47.9)	395 (57.1)				
Age (years)				0.4			0.1
Mean (median)	66.8 (68.0)	66.6 (68.0)	67.2 (69.0)		66.3 (68.0)	67.3 (69.0)	
Range	17–102	17–102	19–99		17–102	19–99	
Age group				<0.001			0.7
≤58	506 (26.9)	300 (25.2)	206 (29.8)		255 (27.8)	251 (26.0)	
59–68	441 (23.4)	306 (25.7)	135 (19.5)		216 (23.5)	225 (23.3)	
69–78	510 (27.1)	364 (30.5)	146 (21.1)		248 (27.0)	262 (27.1)	
≥ 79	427 (22.7)	222 (18.6)	205 (29.6)		199 (21.7)	228 (23.6)	
Race				<0.001			0.08
White	1,595 (87.4)	1,039 (87.2)	556 (80.3)		794 (86.5)	801 (82.9)	
Black	183 (9.7)	73 (6.1)	110 (15.9)		76 (8.3)	107 (11.1)	
Other	106 (5.6)	80 (6.7)	26 (3.8)		48 (5.2)	58 (6.0)	
Socioeconomic status				0.6			0.2
Low	980 (52.0)	626 (52.5)	354 (51.2)		491 (53.5)	489 (50.6)	
High	904 (48.0)	566 (47.5)	338 (48.8)		427 (46.5)	477 (49.4)	
SEER registries				0.3			<0.001
Greater California	274 (14.5)	167 (14.0)	107 (15.5)		156 (17.0)	118 (12.2)	
Atlanta (metropolitan)	65 (3.5)	34 (2.9)	31 (4.5)		21 (2.3)	44 (4.6)	
Connecticut	160 (8.5)	101 (8.5)	59 (8.5)		88 (9.6)	72 (7.5)	
Detroit (metropolitan)	173 (9.2)	114 (9.6)	59 (8.5)		74 (8.1)	99 (10.2)	
Hawaii	41 (2.2)	29 (2.4)	12 (1.7)		17 (1.9)	24 (2.5)	
Iowa	179 (9.5)	125 (10.5)	54 (7.8)		58 (6.3)	121 (12.5)	
Kentucky	93 (4.9)	65 (5.5)	28 (4.0)		53 (5.8)	40 (4.1)	
Los Angeles	266 (14.1)	165 (13.8)	101 (14.6)		134 (14.6)	132 (13.7)	
Louisiana	95 (5.0)	61 (5.1)	34 (4.9)		67 (7.3)	28 (2.9)	
New Jersey	147 (7.8)	91 (7.6)	56 (8.1)		88 (9.6)	59 (6.1)	
New Mexico	77 (4.1)	48 (4.0)	29 (4.2)		39 (4.2)	38 (3.9)	
San Francisco-Oakland	117 (6.2)	62 (5.2)	55 (7.9)		53 (5.8)	64 (6.6)	
San Jose-Monterey	40 (2.1)	27 (2.3)	13 (1.9)		21 (2.3)	19 (2.0)	
Seattle (Puget Sound)	116 (6.2)	76 (6.4)	40 (5.8)		39 (4.2)	77 (8.0)	
Utah	41 (2.2)	27 (2.3)	14 (2.0)		10 (1.1)	31 (3.2)	
Year of primary tumor excision				0.5			<0.001
1988–1996	511 (27.1)	333 (27.9)	178 (25.7)		196 (21.4)	315 (32.6)	
1997–2001	572 (30.4)	361 (30.3)	211 (30.5)		286 (31.2)	286 (29.6)	
2002–2003	334 (17.7)	200 (16.8)	134 (16.4)		182 (19.8)	152 (15.7)	
2004–2006	467 (24.8)	298 (25.0)	169 (24.4)		254 (27.7)	213 (22.0)	

localized stage. Patients within the oldest age group (≥79) had a 3.1 fold ($p < 0.001$) higher mortality rate than their younger age group counterpart (≤58). Interestingly, of all SEER registries, patients from New Mexico had a 1.5-fold higher rate of OM relative to patients from Greater California ($p = 0.03$).

Discussion

Our hypothesis stated that marital status may predispose to more advanced stage and grade at PTE and/or to less favorable cancer-specific, as well as overall survival. We tested this hypothesis in a large population-based cohort from 15 SEER registries ($n = 1{,}884$). All individuals were diagnosed and treated for SCCP between 1988 and 2006.

A previous study examined the effect of MS on stage and grade at presentation and mortality [14]. In that study, the reported rate of married individuals was of 84 %. This percentage reflects higher and more historic marriage rates. Unlike in that previous study, the rate of married individuals was only 63.3 % in our more contemporary cohort. This difference may change the effect of marital status on various cancer-related outcomes. This consideration prompted us to reassess the effect of marital status in a contemporary patient cohort.

In the first part of our analyses, we tested the association between marital status and LASG (T3-4/N1-3/M1/high grade). Our findings revealed that unmarried individuals had a higher rate of LASG SCCP than their married counterparts (57.1 vs. 47.9 %, OR: 1.4, $p = 0.001$) (Table 2). This rate remained significant in multivariable models (OR = 1.5, $p < 0.001$). It is noteworthy that more contemporary year of surgery also exerted a statistically significant effect on the rate of LASG at PTE ($p = 0.01$). Specifically, the rate of LASG SCCP decreased from 32.6 to 22.0 % ($p < 0.001$) between the first (1988–1996) and the most contemporary PTE quartile (2004–2006) (Table 1B).

In the second part of the analyses, we tested whether marital status has an equally important effect on CSM. In univariable survival analyses (Fig. 1), unmarried men had a higher 5-year CSM rate than married men (21.9 vs. 14.8 %, log-rank test: $p = 0.003$). However, when other variables were considered (Table 3B), this relation failed to reach statistical significance (HR = 1.3, $p = 0.1$).

In the final part of the analyses, we examined the relationship between marital status and OM. At 5 years after PTE (Fig. 2), unmarried men were more likely to die, as evidenced by mortality rates of, respectively, 53.8 and 40.9 % (log-rank test: $p < 0.001$). After adjusting for all other covariates (Table 3A), the increased risk of OM for unmarried men persisted and achieved independent predictor status (HR = 1.3, $p = 0.001$).

Table 2 Univariable and multivariable logistic regression models predicting locally advanced versus localized tumor stage and grade at primary tumor excision according to patient characteristics

Predictors	Univariable Odds ratio; 95 % CI	Multivariable Odds ratio; 95 % CI
Marital status		
Reference married		
Unmarried	1.4; 1.20–1.75	1.5; 1.22–1.82
Year of primary tumor excision		
Reference 1988–1996		
1997–2001	0.6; 0.49–0.79	0.7; 0.55–0.92
2002–2003	0.5; 0.39–0.69	0.6; 0.46–0.85
2004–2006	0.5; 0.40–0.67	0.7; 0.49–0.88
Socioeconomic status		
Reference low		
High	1.1; 0.94–1.34	0.8; 0.58–1.01
Race		
Reference White		
Black	1.4; 1.02–1.90	1.4; 1.01–2.01
Other	1.2; 0.81–1.78	1.3; 0.82–2.03
Age group		
Reference ≤ 58		
59–68	1.1; 0.82–1.37	1.0; 0.78–1.33
69–78	1.1; 0.84–1.37	1.1; 0.85–1.42
≥79	1.2; 0.90–1.51	1.1; 0.84–1.44
SEER registries		
Reference greater California		
Atlanta (metropolitan)	2.7; 1.56–4.90	2.3; 1.23–4.14
Connecticut	1.1; 0.73–1.60	1.1; 0.68–1.72
Detroit (metropolitan)	1.8; 1.20–2.60	1.5; 1.01–2.35
Hawaii	1.9; 0.96–3.63	1.8; 0.83–3.86
Iowa	2.8; 1.86–4.09	2.7; 1.75–4.07
Kentucky	1.0; 0.62–1.60	1.0; 0.62–1.64
Los Angeles	1.3; 0.93–1.83	1.0; 0.71–1.48
Louisiana	0.5; 0.34–0.91	0.5; 0.28–0.78
New Jersey	0.9; 0.59–1.33	1.0; 0.64–1.45
New Mexico	1.3; 0.78–2.14	1.0; 0.59–1.70
San Francisco-Oakland	1.6; 1.03–2.47	1.5; 0.92–2.50
San Jose-Monterey	1.2; 0.62–2.33	1.2; 0.61–2.46
Seattle (Puget Sound)	2.6; 1.66–4.11	2.7; 1.62–4.44
Utah	4.1; 1.93–8.69	4.2; 1.92–9.08

CI confidence intervals

Taken together, our findings indicate that unmarried men are predisposed to more unfavorable stage and grade at PTE. However, once the tumor is diagnosed, marital status does not affect CSM. This may imply that tumor biology and treatment are relatively unaffected by marital status. Interestingly, in analyses focusing on OM, the effect of marital status becomes important, even in multivariable

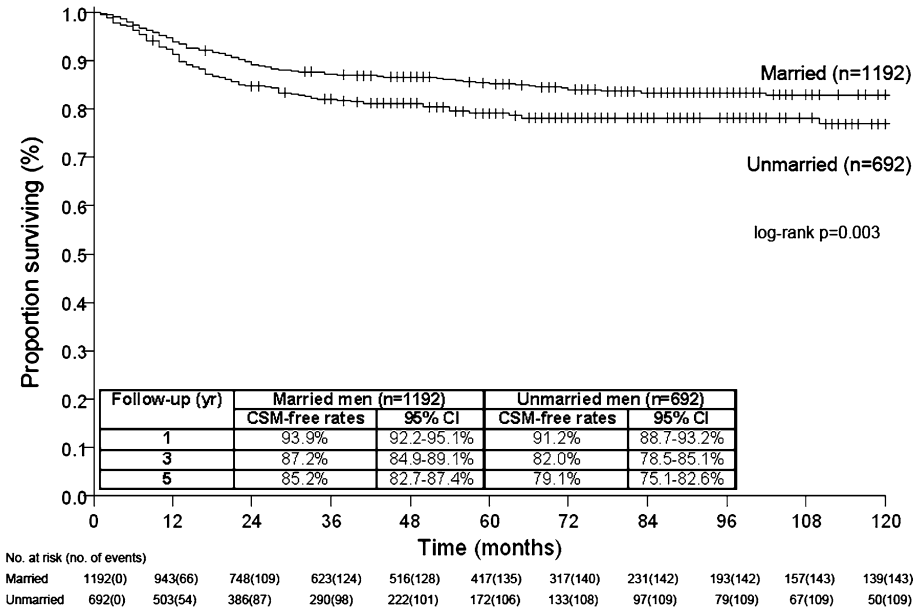

Fig. 1 Kaplan–Meier survival plots for 1,884 patients with squamous cell carcinoma of the penis for cancer-specific mortality-free rates stratified according to marital status

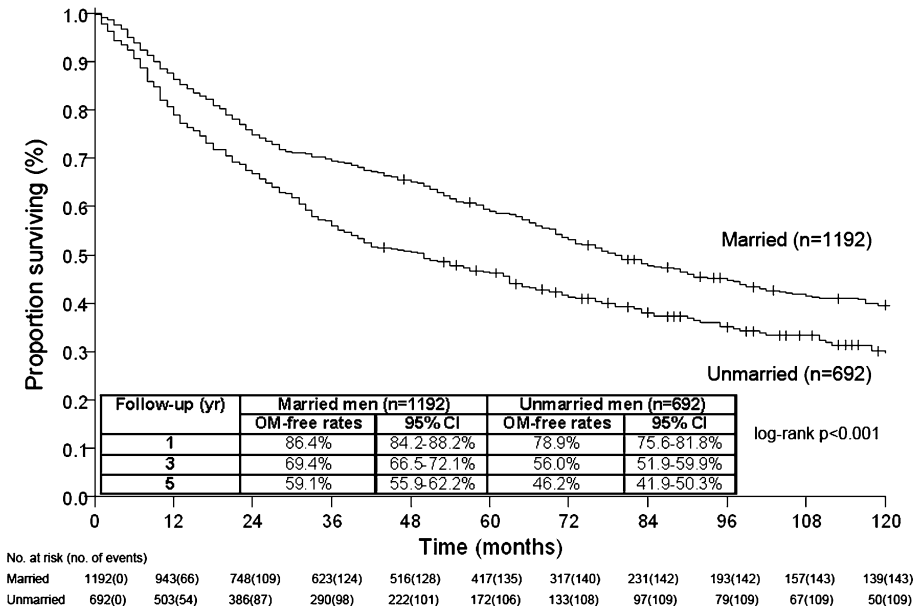

Fig. 2 Kaplan–Meier survival plots for 1,884 patients with squamous cell carcinoma of the penis for overall mortality-free rates stratified according to marital status

analyses, where marital status reached independent predictor status. This may imply that being married predisposes to healthier lifestyle, which in turn translates into increased longevity. Although we could not confirm the independent predictor status of marital status in analyses focusing on CSM, we confirmed the effect of marital status in OM analyses. This implies that marital status may exert a beneficial effect on other endpoints that improve non-cancer-related outcomes.

Several variables may be related to the effect of marital status on more favorable stage and grade at PTE. Married status may encourage men to seek medical help at an earlier stage. This may in turn lead to earlier diagnosis. This hypothesis is consistent with findings from several other tumor sites, such as cervical [3], lung [4], breast [5], and bladder [9] cancers, as well as malignant melanoma [6]. Similarly, as elegantly stated by Gore, married individuals may more closely adhere to routine healthcare visits and screening examinations [9]. This may also contribute to an earlier diagnosis. Additionally, married men may be more likely to benefit a primary health provider than unmarried individuals [25]. Moreover, the effect of spousal intervention may translate into greater compliance with follow-up [27].

Unlike the beneficial effect of marital status on stage and grade at PTE, our results indicate that marital status

Table 3 Univariable and multivariable Cox regression analyses for the prediction of overall mortality [A] and cancer-specific mortality [B] in the entire population ($n = 1{,}884$)

Predictors	[A] Overall mortality			[B] Cancer-specific mortality		
	n events (%)	Univariable HR; 95 % CI	Multivariable HR; 95 % CI	*n* events (%)	Univariable HR; 95 % CI	Multivariable HR; 95 % CI
Marital status						
Reference married	545 (45.7)			143 (12.0)		
Unmarried	377 (54.5)	1.4; 1.24–1.61	1.3; 1.10–1.45	109 (15.8)	1.5; 1.13–1.86	1.3; 0.97–1.62
Stage and grade at presentation						
Reference localized	353 (38.5)			65 (7.1)		
Locally advanced	569 (58.9)	1.7; 1.47–1.91	1.7; 1.52–2.01	187 (19.4)	3.0; 2.30–4.05	3.4; 2.57–4.6
Year of primary tumor excision						
Reference 1988–1996	383 (75.0)			89 (17.4)		
1997–2001	305 (53.3)	1.0; 0.86–1.18	1.1; 0.89–1.25	77 (13.5)	0.8; 0.59–1.08	0.9; 0.62–1.19
2002–2003	130 (38.)	1.0; 0.84–1.28	1.1; 0.86–1.37	49 (14.7)	1.0; 0.71–1.44	1.1; 0.77–1.69
2004–2006	104 (22.3)	1.2; 0.95–1.53	1.3; 0.99–1.66	37 (7.9)	1.0; 0.64–1.42	1.1; 0.70–1.66
Socioeconomic status						
Reference low	466 (47.6)			133 (13.6)		
High	456 (50.4)	0.9; 0.79–1.02	1.0; 0.81–1.18	119 (13.2)	0.9; 0.68–1.12	1.2; 0.80–1.67
Race						
Reference White	792 (49.7)			216 (13.5)		
Black	90 (49.2)	1.1; 0.86–1.33	0.9; 0.74–1.20	23 (12.6)	1.0; 0.65–1.52	0.8; 0.53–1.35
Other	40 (37.7)	0.8; 0.55–1.04	0.9; 0.65–1.34	13 (12.3)	0.9; 0.53–1.61	1.0; 0.52–1.76
Age group						
Reference ≤ 58	176 (34.8)			87 (17.2)		
59–68	186 (42.2)	1.1; 0.88–1.34	1.1; 0.91–1.38	54 (12.2)	0.7; 0.49–0.97	0.7; 0.51–1.02
69–78	256 (50.2)	1.5; 1.27–1.86	1.6; 1.34–1.99	59 (11.6)	0.7; 0.51–0.98	0.7; 0.53–1.03
≥ 79	304 (71.2)	3.1; 2.54–3.70	3.1; 2.56–3.74	52 (12.2)	0.9; 0.61–1.21	0.8; 0.59–1.18
SEER registries						
Reference greater California	93 (33.9)			32 (11.7)		
Atlanta (metropolitan)	38 (58.5)	1.0; 0.68–1.47	1.0; 0.69–1.55	10 (15.4)	1.1; 0.56–2.32	0.9; 0.41–1.87
Connecticut	90 (56.3)	0.9; 0.66–1.20	0.9; 0.63–1.24	23 (14.4)	0.9; 0.53–1.55	0.8; 0.43–1.53
Detroit (metropolitan)	105 (60.7)	1.1; 0.81–1.42	1.1; 0.80–1.47	24 (13.9)	1.0; 0.57–1.66	0.9; 0.49–1.56
Hawaii	15 (36.6)	0.6; 0.35–1.05	0.7; 0.35–1.22	3 (7.3)	0.5; 0.15–1.56	0.4; 0.11–1.51
Iowa	96 (53.6)	0.8; 0.63–1.12	0.8; 0.56–1.05	23 (12.8)	0.8; 0.47–1.38	0.6; 0.34–1.08
Kentucky	24 (25.8)	0.7; 0.44–1.07	0.7; 0.48–1.18	6 (6.5)	0.5; 0.21–1.17	0.5; 0.21–1.23
Los Angeles	142 (53.4)	1.1; 0.83–1.41	1.1; 0.86–1.51	44 (16.5)	1.2; 0.77–1.91	1.2; 0.76–2.00
Louisiana	34 (35.8)	1.1; 0.71–1.56	1.4; 0.92–2.01	7 (7.4)	0.7; 0.29–1.49	1.0; 0.41–2.22
New Jersey	49 (33.3)	0.9; 0.64–1.29	0.9; 0.64–1.31	20 (13.6)	1.1; 0.63–1.93	1.1; 0.63–2.03
New Mexico	53 (68.8)	1.3; 0.91–1.81	1.5; 1.04–2.12	21 (27.3)	2.0; 1.18–3.57	2.2; 1.24–4.01
San Francisco-Oakland	74 (63.2)	1.1; 0.81–1.49	1.1; 0.76–1.52	17 (14.5)	0.9; 0.52–1.70	0.8; 0.40–1.52
San Jose-Monterey	19 (47.5)	0.9; 0.54–1.44	1.0; 0.60–1.68	7 (17.5)	1.2; 0.51–2.63	1.0; 0.42–2.37
Seattle (Puget Sound)	64 (55.2)	0.9; 0.64–1.22	0.8; 0.59–1.21	9 (7.8)	0.5; 0.24–1.04	0.3; 0.15–1.76
Utah	26 (63.4)	1.1; 0.74–1.77	1.0; 0.61–1.55	6 (14.6)	1.0; 0.42–2.40	0.6; 0.25–1.56

HR hazard ratio, *CI* confidence intervals

has no effect on CSM in patients with SCCP. This is not consistent with other urological and non-urological malignancies [6, 10]. For example, married status exerted a protective effect on CSM in patients with bladder cancer and in individuals with malignant melanoma. Disease characteristics may have a profound effect on the relationship between marital status and outcome. Specifically, this may become manifest by higher levels of natural killer cells activation, which may in turn improve cancer control rates independent of the disease [26]. Additionally,

compliance with treatment, delivery of treatment at more highly recognized centers, and more aggressive treatment choices may also result in better cancer control [13]. The discrepancy between SCCP and other malignancies may have to do with a more protracted nature of SCCP in individuals with either localized or locally advanced disease. In localized or locally advanced SCCP, CSM may be low and the effect of marital status on CSM may be difficult to detect and/or to quantify. This appears to have been the case in our study, as marital status emerged as a statistically significant factor in univariable analyses, but not in multivariable models.

Married individuals may benefit added support, information, and financial aid from spouses [24]. All these factors result in a bio-psycho-economical advantage that may correspond to a healthier lifestyle [27, 28]. Additionally, married men are known to avoid risky and/or unhealthy behaviors to a greater extent than unmarried men [29]. Unfortunately, due to the nature of our study, we were not able to directly test these hypotheses.

Our study has several limitations. First, it could benefit a larger sample size and higher power with regard to some borderline significant variables, such as SES. Unfortunately, all previous penile cancer studies relied on even smaller samples ($n = 64$–120) [14–16]. To date, this is the largest studied North American cohort of individuals with SCCP. The assignment of group level SES and income status represents another limitation. Ideally, these variables should be defined according to individual patient characteristics. To adhere to previously reported methodology [21, 22], we relied on an index that combined income, education, and level of poverty within the patient's county of residence. The latter was interpreted as SES. It may be postulated that other more specific SES definitions would have resulted in more statistically significant results.

Although we discriminated between married and unmarried individuals, we could not adjust for other important characteristics within married individuals. These may consist of a previous marriage, quality of life and/or satisfaction of the marriage, duration of marriage, and of several other characteristics. Unfortunately, all previously reported studies were limited by the same considerations [14–16]. Finally, the retrospective nature of the SEER database represents another limitation. Prospective cohort studies could provide better and more specific estimates of the effect of marital status.

Conclusions

Married men tend to present with more favorable stage and grade SCCP. Moreover, married men tend to live longer than their unmarried counterparts. However, marital status has no effect on CSM.

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Conflict of interest The authors declare that they have no conflict of interest.

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