

## Short Communication

# Analysis of Suicide Risk in Patients with Penile Cancer and Review of the Literature

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**Abstract**

**Introduction:** The treatment for penile cancer has been shown to cause harmful psychiatric symptoms as well as have detrimental effects on well-being. In the past several years, alternatives to total or partial penectomy have emerged, such as chemotherapy, radiation, penile sparing, and laser ablation therapies. Since we have published on this topic in general, a more specific breakdown for penile cancer is in order as the therapy has the potential for life changing surgery.

**Materials and methods:** We examined the SEER (1973-2013) database, comprising of 28% of the U.S. population. ICD-10 codes C60.8-C60.9 and the ICD-O codes 8010/2, 8010/3, 8051/2, 8051/3, 8052/2, 8052/3, 8070/2, 8070/3-8072/3, 8074/3, 8076/3, and 8083/3-8084/3 were used. Age, race, marital status, and psychological variables were studied. We used contingency tables of suicide rates; mid-P exact test was used for analysis.

**Results:** There were 13 suicides were noted in 6,155 patients with squamous cell carcinoma of the penis. All patients that committed suicide had undergone a surgical intervention.

**Conclusion:** There is no doubt that penile cancer after treatment has a powerful effect on quality of life as increased depression and sexual anxiety have been continuously documented in post-op patients. This is in stark contrast to the observed suicide rate. Despite the reported negative psychologic effects in patients with penile cancer, suicide rates are amongst the lowest of all urologic malignancies

**ABBREVIATIONS**

HRQOL: Health Related Quality of Life, OR: Odds Ratio, SCC: Squamous Cell Carcinoma

**INTRODUCTION**

Penile cancer is one of the more uncommon urologic cancers. The incidence in Europe and the US is close to 1 in 100,000 men [1,2], while it represents 10-20% of malignancy in men in Africa, Asian, and South America [3]. Squamous cell carcinoma (SCC) makes up > 95% of penile cancers with the most common risk factors being HPV-16, HPV-18, phimosis, smoking, and lower socio-economic status [2,4]. The average age of diagnosis is 60 years and the malignancy is more likely to be seen in men that are not married (OR 2.5) [1,5]. The impact of penile cancer has been shown to cause significant psychological/psychiatric impact.

The treatment for penile cancer varies significantly

depending on cancer stage and has been shown to cause harmful psychiatric symptoms in approximately 50% of patients as well as have detrimental effects on well-being in up to 40% of patients [2]. More aggressive treatments such as a partial penectomy have been shown to cause anxiety in 31-58% of patients and depression in 39% of patients [6,7] with significantly higher rates of anxiety in patients treated with a total penectomy [8]. Much of these psychological/psychiatric effects are thought to be secondary to the devastating effect on a man's self-image and sexual function [7,9]. For that reason, modalities such as penile sparing surgical approaches, chemotherapy/radiation protocols, and laser ablative surgeries have been investigated as options to sexuality and HRQOL [9-11].

Approximately 70% of suicides in the elderly (> 60 years-old) are attributed to physical illness and malignancy [12]. We sought to investigate the risk of suicide in patients with penile cancer.

## MATERIALS AND METHODS

### Data sources

Patients with penile cancer were identified from the Surveillance, Epidemiology, and End Results (SEER) database. The SEER database reports cancer-specific outcomes from specific geographic areas representing 28% of the US population [13]. The study cohort consisted of patients from all 18 registries comprising SEER from 1973 through 2013. Comparisons with the general US population were based on data from the Centers for Disease Control and Prevention's National Center for Injury Prevention and Control (1999-2010) [14].

### Study population

Patients were identified in the SEER database using the primary site code C60.8-C60.9 for penile cancer. To increase generalizability, squamous cell carcinoma histology for penile cancer was identified using International Classification of Diseases for Oncology (ICD-O) codes, specifically ICD-O codes 8010/2, 8010/3, 8051/2, 8051/3, 8052/2, 8052/3, 8070/2, 8070/3-8072/3, 8074/3, 8076/3, and 8083/3-8084/3.

### Description of variables

Demographic variables of interest included age at the time of diagnosis (by decade), race (African American vs white vs other), and marital status (married vs single/divorced/widowed [SDW]). Clinical and pathologic variables included disease SEER histologic grade, and SEER stage (localized vs regional vs distant vs unstaged). Previous studies have determined important psychosocial/environmental risk factors for suicide, including but not limited to heavy alcohol and drug use, perceived sadness/

hopelessness, low academic achievement, poor perceived health status, and high perceived stress [15]. Given the variables available in the SEER database, only the aforementioned demographic, clinical, and pathologic variables were used for the current analysis. The primary outcome was suicide (yes/no). Patients were considered to have committed suicide as previously described [16]. Overall survival was calculated for those dead of suicide (DOS) and those dead of causes other than suicide (DOC). Contingency tables of suicide rates were calculated as previously described [3]. Standardized mortality ratios (SMRs) and 95% confidence intervals (95% CIs) were calculated using the mid-P exact test as previously described [17]. Briefly, suicide rates (number of suicides divided by person-years of survival) were calculated to allow comparison between the anatomic cancer site and the general population [14,16]. Calculated SMRs for the US population based on age ranges 58-77 years) [14].

## RESULTS

There were suicides identified among 1,239,522 individuals with genitourinary malignancies observed for 7,307,377 person-years. There were 13 suicides out of 6,155 patients with penile cancer (SMR, 1.58; 95% CI, 1.18-2.11) (Table 1). Of the 6,155 patients with penile cancer, 5,569 underwent surgical treatment for their disease. 593 patients chose to undergo adjuvant or solitary radiation therapy. All 13 suicides recorded were amongst those who had undergone a surgical intervention (partial penectomy, total penectomy, etc) and 1 who had undergone adjuvant radiation. The median overall survival for penile cancer for DOS was 37 months and for DOC was 25 months. All patients who committed suicide were between the ages of 50-79 years of age. 11 patients were married while 2 were SDW.

**Table 1:** Incidence of Suicide Among Patients with Penile Cancer by Demographic Characteristics (1973-2013).

Factor	Persons	Number of Suicides	Person-Years	Suicide Rates per 100,000 Person-Years	SMR	95% CI
Population	6,155	13	34,197	38	1.58	1.18-2.11
≤ 39	248	0	2,067	0	-	-
40-49	558	0	4,745	0	-	-
50-59	1,020	5	7,409	67	2.56	2.04-3.19
60-69	1,575	5	9,138	55	2.43	1.88-3.08
70-79	1,602	3	7,620	39	1.39	1.04-1.84
≥ 80	1,152	0	3,218	0	-	-
Marital Status						
Married	3,556	11	22,269	49	2.05	1.57-2.64
SDW	2,154	2	9,712	21	0.84	0.56-1.21
Unknown	445	0	2,216	0	-	-
Race						
African American	607	0	3,114	0	-	-
Caucasian	5,221	13	29,270	44	1.67	1.26-2.17
Other	270	0	1,490	0	-	-
Unknown	57	0	322	0	-	-

Abbreviations: 95% CI, 95% confidence interval; SDW, single/divorced/widowed; SMR, standardized mortality ratio.

<sup>a</sup>Compared with suicide rates of the general US population according to the Centers for Disease Control and Prevention's Web-based Injury Statistics Query and Reporting System (WISQARS) (1999-2010).

As with other malignancies, there was an increased risk of suicide in white patients and with advancing age with penile cancer (Table 1). Unlike other malignancies in which suicide risk is greater in advanced stage and grade and in single/divorced/widowed patients, penile cancer demonstrated an inverse association with cancer stage/grade (Table 2) and marital status (Table 1).

## DISCUSSION AND CONCLUSION

Although more prevalent in underdeveloped countries, penile cancer is a rare urologic disease in the US and European countries. Analysis of the SEER database from 1998-2003 found 4967 cases of penile cancer with an incidence of 0.81 per 100,000 white males and 0.82 per 100,000 African American males.<sup>11</sup> Surgical treatment of penile cancer causes harmful psychiatric symptoms in approximately 50% of patients as well as have detrimental effects on well-being in up to 40% of patients.<sup>2</sup> Varying treatment modalities affected sexual health, assessed most commonly by the IIEF-15, differently and are associated with different degrees of psychological impact (Table 3).

Both penile sparing and laser ablative therapies with the YAG laser are associated with fewer psychiatric effects. This is likely due to the fact that patients undergoing penile sparing surgery

recover similar sexual function (as high as 72%) and have a satisfactory HRQOL [10,11]. Kieffer et al., found that patients who underwent penile sparing (n=54) there were few differences in HRQOL compared to the normative population and they also suffered from less problems with life interference and body image when compare to patient who underwent a partial penectomy [9]. Therapies such as the YAG laser (combined carbon dioxide and neodymium) can be considered in patient with Tis-T2, GI-II tumors less than 3cm (95% cancer specific survival at 5 yrs) with low recurrence rates (19%) [14].

Partial penectomy, commonly reserved for tumors confined to the glands or distal shaft, has been shown in the literature to have mixed psychiatric/psychologic effects. Many articles, using the IIEF-15, have reported significant impairment in erectile function, orgasmic function, sexual desire, intercourse satisfaction, overall sexual satisfaction, and body image [6-8,18]. Yu et al., conducted a prospective study of 43 men with penile cancer undergoing partial penectomy in 2015; they assessed pre- and post-operative sexual health using the IIEF-15 and found there to be a significant difference in each domain of the survey. Furthermore, patients undergoing partial penectomy were found to higher levels of anxiety and depression (as high as 58% and 39% respectively) [6,8,18]. Individuals with proximally invasive

**Table 2: Incidence of Suicide Among Patients With Penile Cancer by Clinicopathologic Characteristics**

Factor	Persons	Number of Suicides	Person-Years	Suicide Rates per 100,000 Person-Years	SMR	95% CI
Grade						
Well differentiated; Grade I	1,609	4	10,708	37	1.55	1.15-2.07
Moderately differentiated; Grade II	2,163	3	10,438	29	1.17	0.82-1.60
Poorly differentiated; Grade III	1,011	2	4,002	50	2.01	1.53-2.56
Undifferentiated; Anaplastic; Grade IV	43	0	209	0	-	-
Unknown	1,329	4	8,840	45	1.84	1.41-2.41
Stage						
Localized	3,774	10	24,186	41	1.71	1.29-2.26
Regional	1,771	3	3,494	86	3.42	2.78-4.14
Distant	295	0	452	0	-	-
Unstaged	315	0	1,566	0	-	-
Surgery Performed						
Yes	5,569	13	32,167	40	1.62	1.22-2.14
No	535	0	1,789	0	-	-
Unknown	51	0	241	0	-	-
Radiation Performed						
Yes	593	1	2,761	36	1.5	1.11-2.02
No	5,481	12	31,121	39	1.57	1.16-2.08
Unknown	81	0	314	0	-	-

Abbreviations: 95% CI, 95% confidence interval; RPLND, retroperitoneal lymph node dissection; SMR, standardized mortality ratio.

<sup>a</sup>Compared with suicide rates of the general US population according to the Centers for Disease Control and Prevention's Web-based Injury Statistics Query and Reporting System (WISQARS) (1999-2010).

**Table 3:** Studies reviewed for psychological/psychiatric effects of penile cancer.

Author	Sample Size	Mean Age	Design	Intervention	Parametric Tool	Findings
Yu et al., 2016 <sup>6</sup>	43	56	Prospective	Partial Pen (n= 43)	IIEF-15 SAS SDS	Pre and Postop IIEF-15 scores were significantly different in each domain. Postop Anxiety and depression seen in 58% and 39% respectively
Kieffer et al., 2014 <sup>9</sup>	90	65.4	Retrospective	Penile sparing (n=54) Partial Pen (n=36)	SF-36 IIEF-15 IOC (version 2)	Few differences were observed in sexuality or health related QOL compared to normative population. Partial Pen associated with more problems with life interference and body image
Novac et al., 2013 <sup>8</sup>	11	62.9	Retrospective	Total Pen (n=2) Partial Pen (n=6) Biopsy (n=3)	HAM-A HAM-D	Moderate-Severe depression in both partial and total penectomy groups. Sig higher Anxiety in total penectomy compared to partial (p=0.02)
Gulino et al., 2007 <sup>10</sup>	14	54	Prospective	Penile sparing (n=14)	IIEF-15 Bigelow & Young	Recovery of similar sexual function compared to preop. Satisfactory QoL
Romero et al., 2005 <sup>7</sup>	18	52	Retrospective	Partial Pen (n= 18)	IIEF-15	Erectile function, orgasmic function, sexual desire, intercourse satisfaction, overall sexual satisfaction were significantly reduced
Windahl et al., 2004 <sup>11</sup>	40	64	Retrospective	YAG laser ablation (n=40)	IIEF-11 LiSat-11 Self made sexual function Self made sexual activity	Sexual function and satisfaction only marginally reduced compared to preop. 72% with sex life as good as they wanted,
Ficarra et al., 2000 <sup>18</sup>	16	n/a	Retrospective	Partial Pen (n=14)	HADS GHQ	Significant impairment of the general state of health and higher levels of anxiety compared to control

**Abbreviations:** GHQ: General Health Questionnaire; HAM-A: Hamilton Anxiety Rating Scale, HAM-D: Hamilton Rating Scale for Depression; IOC: Impact of Cancer (Version 2); IIEF-15: International Index of Erectile Function; LiSat-11: Life Satisfaction in 18- to 64-year-old Swedes; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; SF-36: Short Form -36 Health Survey

penile cancer requiring a total penectomy have significantly higher anxiety levels compared to those undergoing a partial penectomy [8].

Malignancy has been shown to be a significant cause of suicide in those greater than 60 years old. Our prior analysis of the SEER database from 1973-2013, we found 2276 suicides in patients with urologic cancer (Prostate cancer: 1613, Bladder cancer: 439, Kidney cancer: 140, Testis cancer: 71, Penile cancer: 13). Despite all the detrimental psychological effects that treatments for penile cancer have, only 13 of the 2276 patients that committed suicide had penile cancer. The current analysis shows that those patients committing suicide with penile cancer also do not follow trends observed for other malignancies, particularly the fact that penile cancer patients with low grade and stage were more likely to commit suicide. This fact contradicts many of the studies in the literature reporting improved HRQOL with lower grade and stage tumors treated conservatively (Table 3).

Although the literature reports mixed effects on men's HRQOL and sexual health, the overwhelming majority of articles analyzing those who underwent partial or total penectomy reported significant increases in anxiety and depression and significant decreases in sexual health. This topic has been investigated more thoroughly in penile cancer than any other urologic cancer. In our retrospective analysis, all 13 patients had undergone some form of surgical intervention of unknown approach. However,

despite all the detrimental effects reported, penile cancer has not been shown to cause increased risk for suicide compared to other urologic malignancies. One explanation for this may be the fact that penile cancer is so rare and therefore more retrospective studies of large databases should be carried out.

## REFERENCES

- Hernandez BY, Barnholtz-Sloan J, German RR, Giuliano A, Goodman MT, King JB, et al. Burden of invasive squamous cell carcinoma of the penis in the United States, 1998-2003. *Cancer*. 2008; 113: 2883-2891.
- Maddineni SB, Lau MM, SangarVK. Identifying the needs of penile cancer sufferers: a systematic review of the quality of life, psychosexual and psychosocial literature in penile cancer. *BMC Urol*. 2009; 9: 8.
- Ornellas AA. Management of penile cancer. *J SurgOncol*. 2008; 97: 199-200.
- Miralles-Guri C, Bruni L, Cubilla AL, Castellsagué X, Bosch FX, de Sanjosé S. Human papillomavirus prevalence and type distribution in penile carcinoma. *J Clin Pathol*. 2009; 62: 870-878.
- Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in situ and invasive disease. *Int J Cancer*. 2005; 116: 606-616.
- Yu C, Hequn C, Longfei L, Minfeng C, Zhi C, Feng Z, et al. Sexual Function after Partial Penectomy: A Prospectively Study From China. *Sci Rep*. 2016; 6: 21862.

7. Romero FR, Romero KR, Mattos MA, Garcia CR, Fernandes Rde C, Perez MD. Sexual function after partial penectomy for penile cancer. *Urology*. 2005; 66: 1292-1295.
8. Novac B, Ciobica A, Dobrin R, Ciobotaru M, Costache C. Psychological/psychiatric trauma in patients with penile cancer and partial or total penectomy. *Arch Biol Sci*. 2013; 65: 1293-1298.
9. Kieffer JM, Djajadiningrat RS, van Muilekom EA, Graafland NM, Horenblas S, Aaronson NK. Quality of life for patients treated for penile cancer. *J Urol*. 2014; 192: 1105-1110.
10. Gulino G, Sasso F, Falabella R, Bassi FB. Distal urethral reconstruction of the glans for penile carcinoma: results of a novel technique at 1-year of follow-up. *J Urol*. 2007; 178: 941-944.
11. Windahl T, Skeppner E, Andersson SO, Fugl-Meyer KS. Sexual function and satisfaction in men after laser treatment for penile carcinoma. *J Urol*. 2004; 172: 648-651.
12. Schneider RK. The suicidal patient. In: McKean SC, Ross JJ, Dressler DD, Brotman DJ, Ginsberg JS, eds. *Principles and Practice of Hospital Medicine*. New York: McGraw-Hill; 2002: 1915-1920.
13. National Cancer Institute. *Surveillance, Epidemiology and End Results (SEER)*, 2013. Bethesda, MD: National Cancer Institute; 2013.
14. Hoyert DL, Heron MP, Murphy SL, Kung HC. Deaths: final data for 2003. *Natl Vital Stat Rep*. 2006; 54: 1-120.
15. Kim SM, Baek JH, Han DH, Lee YS, Yurgelun-Todd DA. Psychosocial-environmental risk factors for suicide attempts in adolescents with suicidal ideation: findings from a sample of 73,238. *Suicide Life Threat Behav*. 2015; 45: 477-487.
16. Misono S, Weiss NS, Fann JR, Redman M, Yueh B. Incidence of suicide in persons with cancer. *J Clin Oncol*. 2008; 26: 4731-4738.
17. Ury HK, Wiggins AD. Another shortcut method for calculating the confidence interval of a Poisson variable (or of a standardized mortality ratio). *Am J Epidemiol*. 1985; 122: 197-198.
18. Ficarra V, Righetti R, D'Amico A, Piloni S, Balzarro M, Schiavone D, et al. General state of health and psychological well-being in patients after surgery for urological malignant neoplasms. *Urol Int*. 2000; 65: 130-134.
19. Klaassen Z, Jen RP, DiBianco JM, Reinstatler L, Li Q, Madi R, et al. Factors associated with suicide in patients with genitourinary malignancies. *Cancer*. 2015; 121: 1864-1872.

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