

Obesity and Invasive Penile Cancer

Known risk factors for invasive penile cancer include lack of neonatal circumcision, poor genital hygiene, phimosis, human papilloma virus infection, race, and tobacco use [1]. We have observed that penile cancer patients tend to be more obese than patients without penile cancer. Obese penile cancer patients tend to present at later stages of the disease compared with nonobese penile cancer patients. We hypothesize that obesity may impair genital self-examination, genital cleansing, and physician examination, which may lead to both increased risk of penile cancer and a delayed recognition of symptoms that leads to presentation at a more advanced stage. We conducted a case series and a case-control study to evaluate the association between invasive penile cancer and obesity.

The University of Iowa is the only academic medical center in Iowa and serves as the tertiary referral center. Upon institutional review board approval, we identified all men diagnosed with invasive penile squamous cell carcinoma (1974–2011) through the University of Iowa Hospitals and Clinics' Cancer Registry and extracted clinical data by retrospective chart review. Height and weight closest to the time of diagnosis were used to calculate body mass index (BMI). The American Joint Committee on Cancer 2010 staging system was used to classify cancer stage. Records for 110 patients with invasive penile cancer were available, with clinical information available for analysis on 101 patients. Multivariate ordinal logistic regression was used to examine the association between BMI and stage at diagnosis while controlling for age at diagnosis, circumcision, and smoking.

Population-based, cancer-free controls were identified through the Iowa section of the Behavior Risk Factor Surveillance System (BRFSS), a state-based, cross-sectional, telephonic survey that collects information on health risk behaviors, preventive practices, and health care access [2]. As the Iowa BRFSS started in 1988, only cases diagnosed after 1984 were used in this analysis. Seventy-seven penile cancer cases were matched to 12 420 controls within 61 strata determined by age and year of diagnosis (5-yr strata for both), race, and smoking status. Conditional logistic regression was used to examine the association between BMI and odds of invasive penile cancer.

The mean BMI for the 101 penile cancer cases was 31.8 (Table 1). Higher BMI was associated with worse stage at diagnosis. On multivariate ordinal logistic regression, every 5-unit increase in BMI was associated with 49% increased odds of higher stage at diagnosis (odds ratio [OR]: 1.49; 95% confidence interval [CI], 1.16–1.91; $p = 0.002$). On conditional logistic regression, the odds of invasive penile cancer increased with increasing BMI (OR: 2.0; 95% CI, 1.72–2.33; $p < 0.001$, per 5-unit increase in BMI).

We found consistent associations between BMI and penile cancer. Higher BMI was associated with both an increased risk of developing invasive penile cancer and a more advanced cancer stage at presentation. The biologic

mechanism for this increased risk is unknown but might be mediated by impaired genital hygiene because of obesity. Obesity can hamper genital self-examination and cleansing and can cause a buried penis with resultant smegma accumulation and functional phimosis. Obesity may also impair examination by health care providers, which may lead to delayed recognition of symptoms that leads to presentation at a higher stage. Obesity has been associated with other cancers, including cancer of the colon, postmenopausal breast, endometrium, kidney, and esophagus. Other obesity-associated carcinogenesis mechanisms such as chronic inflammation, oxidative stress, and insulin resistance may also play a role in the development of penile cancer [3].

This study is limited by its retrospective design and the possibility of selection bias and limited generalizability because of referral patterns at an academic medical center. The chart review spanned more than three

Table 1 – Characteristics of 101 penile cancer patients

Characteristic	Result
Age	
Yr, mean (SD)	62.23 (13.0)
Yr, range	30.1–84.4
BMI	
m/kg ² , mean (SD)	31.8 (8.3)
m/kg ² , range	18.2–66.9
Race, patients, no.	
White	86
Hispanic	6
Native American	2
Other	3
Unknown	4
Smoking status, patients, no.	
Current smoker	42
Nonsmoker	27
Former smoker ^a	28
Unknown	4
Circumcised, patients, no.	
Yes	19
No	57
Unknown	25
AJCC stage, patients, no. ^b	
1	45
2	27
3	16
4	13
Histologic grade, patients, no.	
Well differentiated	32
Moderately differentiated	44
Poorly differentiated	14
Unknown	11
AJCC stage, BMI, m/kg ² , median (range)	
1	28.6 (19.3–48.8)
2	29.9 (18.2–40.7)
3	33.6 (24.4–55.5)
4	32.0 (26.8–66.9)

SD = standard deviation; BMI = body mass index; AJCC = American Joint Committee on Cancer.

^a Patients who stopped smoking ≥ 1 yr prior to diagnosis were considered former smokers.

^b Stage 1: tumors invasive into the subepithelial connective tissue of the penis; stage 2: tumors invade corpus spongiosum, cavernosum, or urethra; stage 3: tumors metastatic to inguinal lymph nodes; stage 4: tumors metastatic to pelvic lymph nodes or distant sites.

decades, so we did not have data on phimosis, human papillomavirus infection, or the timing of circumcision. Being a rare malignancy, penile cancer is difficult to study even at large referral centers and necessitates retrospective studies. Our study is strengthened by the use of population-based controls and by observation of consistent associations in both the case series and the case–control studies.

Therapeutic options for advanced penile cancer are limited, and mortality is high [4]. Successful control of obesity might prevent development of penile cancer and lead to earlier diagnosis, when treatment is more effective.

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Daling J, Madeleine M, Johnson L, et al. Penile cancer: importance of circumcision, HPV and smoking in in situ and invasive disease. *Int J Cancer* 2005;116:606–16.
- [2] Edge SB, Byrd DR, Compton CC, et al. *AJCC cancer staging manual*. ed 7. New York, NY: Springer; 2010.
- [3] Basen-Engquist K, Chang M. Obesity and cancer risk: recent review and evidence. *Curr Oncol Rep* 2011;13:71–6.
- [4] Rippentrop JM, Joslyn SA, Konety BR. Squamous cell carcinoma of the penis: evaluation of data from the Surveillance, Epidemiology and End Results Program. *Cancer* 2004;101:1357–63.

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