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Original article

Incidence trends in primary malignant penile cancer☆

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Abstract

Objective: To examine trends in the incidence of primary, malignant penile cancer in the United States.

Methods and materials: A total of 1,817 men with primary, malignant penile cancer diagnosed between 1973 and 2002 from the Surveillance, Epidemiology and End Results Program Public-use data were used for analysis. Incidence rates were calculated by clinical and demographic variables of interest and decade of diagnosis (1973–1982, 1983–1992, and 1993–2002) using Surveillance, Epidemiology and End Results-Stat 6.1, and trends were examined using the annual percent change statistic. Additional incidence calculations were performed to examine further racial/ethnic differences.

Results: The overall incidence of primary, malignant penile cancer from 1973 to 2002 was 0.69 per 100,000. Incidence decreased significantly over time: 0.84 per 100,000 in 1973–1982 to 0.69 per 100,000 in 1982–1992 to 0.58 per 100,000 in 1993–2002. Incidence increased with increasing age at diagnosis. The majority of cases had squamous cell carcinomas, graded as I or II, and originated at the glans penis. Incidence of unknown grade primary, malignant penile cancer decreased significantly over the last 30 years, as did incidence of primary site penis, not otherwise specified primary, malignant penile cancer. The incidence of regional stage disease also increased over time. From 1993 to 2002, White Hispanics had the highest incidence rates (1.01 per 100,000) followed by Alaska Native/American Indians (0.77 per 100,000) and Blacks (0.62 per 100,000).

Conclusions: The overall incidence of primary, malignant penile cancer in the United States has decreased, and these rates varied by race/ethnicity. Incidence rates increased with increasing age at diagnosis, and the incidence of regional stage disease increased over time, while incidence of unknown grade primary, malignant penile cancer decreased over the last 30 years.

Keywords: Penile cancer; Incidence rates; Time trends; Race/ethnicity; Surveillance, Epidemiology and End Results (SEER)

1. Introduction

Primary, malignant penile cancer is a rare disease representing 0.3% to 0.5% of U.S. male malignancies [1]. Penile cancer incidence in developed countries, such as the United States or Europe, is less than 1.00 per 100,000 [2]. In 2006, it is estimated that there will be 1,530 new cases of penile and other male genital cancers diagnosed in the United States [3]. Worldwide geographic variation in primary, malignant penile cancer incidence is evident and could be caused, in part, by differences in hygienic, social, and religious practices [4].

There have been a number of risk factors identified for primary, malignant penile cancer, including circumcision, tobacco use, and human papillomavirus (HPV) status [5–8]. The strongest, most consistently reported risk factor associated with an increased risk of disease is a lack of neonatal circumcision [6,7]. More recently, primary, malignant penile cancer has been associated with the presence of the HPV, which was present in 15% to 80% of patients with primary, malignant penile cancer and thought to account for 50% of all penile cancers [9,10]. Prognosis after penile cancer diagnosis is very good, with only an estimated 280 deaths occurring in 2006 [3], and is significantly affected by stage, grade, and lymph node involvement.

Our knowledge to date about primary, malignant penile cancer is largely from case series studies at single institu-

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tions only, making generalizability of these data difficult. The current literature lacks definitive population-based data on the overall incidence of primary, malignant penile cancer as well as trends over time. Therefore, our study objective was to characterize overall primary, malignant penile cancer incidence and trends in it in the United States using a population-based data set. The Public-Use data from the population-based Surveillance, Epidemiology and End Results (SEER) Program is an easily obtainable population-based data set of incident cancer cases diagnosed between 1973 and 2002 in the United States. These data cover approximately 26% of the United States and are thereby representative of the greater U.S. population [11]. Using population-based data allows for unbiased estimates and generalizability of results to the entire U.S. population.

2. Materials and methods

2.1. Study population

A total of 1,817 men with primary, malignant penile cancer diagnosed between 1973 and 2002 from the SEER Public-use data using cases from the SEER 9 registries were used for analysis. The SEER Program is a national cancer surveillance program established by the National Cancer Institute that collects data on all incident cancer cases from 14 population-based cancer registries and 3 supplemental registries covering approximately 26% of the U.S. population [11], representative of national demographic characteristics. Local institutional review board approval was not needed for the analysis of these data because they were de-identified and publicly available.

2.2. Case selection

Overall, there were a total of 2,010 primary, malignant penile cancer cases diagnosed between 1973 and 2002 (i.e., first primary malignant penile tumors only). Primary, malignant penile cancer cases were further selected using the following inclusion criteria: reporting sources were inpatient/outpatient hospital or clinic, hospital or private laboratory, physician office or private medical practitioner and nursing/convalescent home or hospice only; the cancer diagnosis was microscopically confirmed and primary, malignant penile cancer histology was either squamous cell carcinoma or verrucous carcinoma, not otherwise specified (NOS). All ages at diagnosis were included.

2.3. Variables of interest

Year of diagnosis was divided into 3 decade-long intervals: 1973–1982 (first decade), 1983–1992 (second decade), and 1993–2002 (third decade). Variables of interest were age at diagnosis, race/ethnicity, histologic type of tumor, grade of tumor, primary site of tumor, SEER historical stage of tumor, and SEER registry site. Age at diagnosis was grouped into 7 categories: younger than 35 years, 35–44 years, 45–54 years, 55–64 years, 65–74 years, 75–84 years, and 85 years and older. Race was categorized as White, Black, other, and unknown. Other was defined as American Indian/Alaska Native or Asian/Pacific Islander. Ethnicity was defined as Hispanic or non-Hispanic. Tumor histology was classified into 1 of the following 2 categories using 4-digit International Classification of Disease-Oncology (ICD-O) codes: squamous cell carcinoma (8070, 8071, 8076, 8052, 8072, 8074, and 8075) or verrucous carcinoma, NOS (8051). Tumor grade was defined as: well or moderately differentiated (grade I and II); poorly differentiated or undifferentiated, anaplastic (grade III and IV); or unknown. Primary tumor site was also categorized using ICD-O codes: prepuce (C60.0), glans penis (C60.1), body of penis (C60.2), overlapping lesion (C60.8), or penis, NOS (C60.9). The SEER historical stage of tumor was classified as localized, regional, distant, and unstaged.

2.4. Statistical analysis

Overall frequencies and frequencies by decade of diagnosis were calculated for all variables of interest. Overall incidence rates and rates by decade of diagnosis, and their 95% confidence intervals (CIs), were calculated for each variable of interest using SEER-Stat 6.1 [12]. All incidence calculations were age-adjusted to the 2000 U.S. standard population and shown per 100,000 persons. Incidence trends over time were tested for statistical significance using the annual percentage change statistic, indicating an increased or decreased trend with a 2-sided P value. In addition, 95% CIs were compared by decade of diagnosis, and if the CIs did not overlap, then a significant difference ($P \leq 0.05$) in incidence rates by decade of diagnosis was noted.

2.5. Racial/ethnic differences in incidence

To investigate further racial/ethnic variation in incidence of primary, malignant penile cancer, specifically, differences between Hispanics and non-Hispanics (i.e., ethnicity), it was necessary to use the SEER 13 Public-Use data instead of the SEER 9 data. Population files with Hispanic status information were only available for the SEER 13 data for cases diagnosed 1992–2002. However, population files with race information were available for all years of diagnosis (1973–2002). Therefore, cases from the SEER 13 data diagnosed 1993–2002 were chosen to compare them directly with the SEER 9 third-decade data calculations by race only (White, Black, and other). Using the further available information on ethnicity (Hispanic/non-Hispanic) in the SEER 13 data allowed for calculation of incidence rates for additional racial/ethnic categorizations: (1) White non-Hispanic, White Hispanic, non-White, non-Hispanic, and non-White Hispanic (SEER 13 without the Alaska Native Tumor Registry);