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Scrotal Cancer Incidence Rates and Trends—United States, 1999–2020

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Abstract

Objective—To examine population-level scrotal cancer incidence rates and trends among adult men in the United States.

Methods—Data from the United States Cancer Statistics, covering approximately 96% of the United States population, were analyzed to calculate age-standardized incidence rates of scrotal cancer among men aged 18 years and older from 1999 to 2020. Trends in incidence rates were evaluated by age, race and ethnicity, Census region, and histology using joinpoint regression.

Results—Overall, 4,669 men were diagnosed with scrotal cancer (0.20 per 100,000). Incidence rates were highest among men aged 70 years and older (0.82 per 100,000). Rates were higher among non-Hispanic Asian or Pacific Islander men (0.31 per 100,000) compared to other race and ethnicity groups. The most common histologic subtypes were squamous cell carcinoma (35.9%), extramammary Paget disease (20.8%), and sarcoma (20.5%). Incidence rates decreased by 2.9% per year from 1999 to 2019 for non-Hispanic Asian or Pacific Islander men, decreased by 8.1% per year from 1999 to 2006 for basal cell carcinomas, and increased by 1.8% per year from 1999

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Appendix A. Supplementary material

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

to 2019 for extramammary Paget disease; otherwise, rates remained stable for all other variables examined.

Conclusion—While scrotal cancer incidence rates were higher than previously reported, rates were still low and stable over time.

Keywords

Genital cancer; incidence rates; incidence trends; joinpoint regression; rare cancers; scrotal cancer; scrotum

INTRODUCTION

Scrotal cancers are rare male malignancies,[1] and the current literature on its incidence is limited. In an analysis of Surveillance, Epidemiology, and End Results (SEER) Program data from the United States, scrotal cancer incidence rates nearly doubled from 0.049 per 100,000 in 1973 to 0.095 in 2002.[2] Scrotal cancers have historically been associated with occupational exposures,[1–3] but improvements in industrial hygiene have reduced these types of exposures in recent years. Therefore, the increase in scrotal cancer incidence may suggest other risk factors, such as iatrogenic conditions and human papillomavirus (HPV) infection, varying depending on histologic type.[1] Notably, emerging evidence suggests an etiologic role of HPV in the development of scrotal squamous cell carcinoma (SCC).[4–6] Given the increasing incidence from 1973 to 2002, lack of recent research, and possible link with HPV, we examined scrotal cancer incidence rates and trends among adult men in the United States.

METHODS

Data

We analyzed population-based central cancer registry data from the United States Cancer Statistics database, which combines data from the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's SEER Program.[7] Cancer registry data were collected using uniform data items and codes and met the United States Cancer Statistics publication criteria, covering 95.8% of the United States population from 1999 to 2020.[8]

Cancer definition

Histologically confirmed cases of primary scrotal cancer were defined using the *International Classification of Diseases for Oncology*, Third Edition (ICD-O-3), site code C63.2, excluding histology codes 9050–9055 (mesothelioma), 9140 (Kaposi sarcoma), and 9590–9992 (lymphoma, myeloma, and leukemia).

Study variables

Scrotal cancer incidence rates were examined by age, race and ethnicity, Census region, stage, and histology. Race and ethnicity were grouped into 5 mutually exclusive groups: non-Hispanic White, non-Hispanic Black, non-Hispanic American Indian or Alaska Native,

non-Hispanic Asian or Pacific Islander, and Hispanic. Geographic area was categorized into 4 United States Census regions: West, Northeast, Midwest, and South. Stage was classified as early, late, and unknown or unstaged using a merged variable that spans the periods when three different staging schemes were used (SEER Summary Stage 2000, Derived SEER Summary Stage 2000, and Summary Stage 2018). Histology was categorized using the following ICD-O-3 morphology codes: SCC (8050–8084, 8120–8131), extramammary Paget disease (8542–8543), sarcoma (8800–9043, 9120–9260, 9540), basal cell carcinoma (8090–8102), adenocarcinoma (8140–8490,8560–8574), melanoma (8720–8773), and other (8000–8041, 8247, 9473–9500). As sensitivity analysis, incidence rates were also analyzed excluding extramammary Paget disease and sarcoma subtypes.

Statistical analyses

Incidence rates were age-standardized to the 2000 United States standard population by direct method[9] and expressed per 100,000 men. The corresponding 95% confidence intervals (CI) were calculated as modified gamma intervals.[10] Rate ratios and 95% CI were calculated to assess the relative differences in incidence rates. We examined incidence rates from 1999 to 2020 and trends from 1999 to 2019 to avoid any potential impact of the COVID-19 pandemic on cancer diagnosis and reporting.

Trends in incidence rates were calculated using joinpoint regression and quantified using annual percent change (APC).[11] As the APC and average annual percent change were similar, we report only APC estimates in this paper. If the APC differed from zero at an alpha of 0.05, we considered incidence rates to increase or decrease; otherwise, rates were reported as stable. We used the weighted Bayesian information criterion for model selection and the empirical quantile method to calculate 95% CI for APC. We calculated age-standardized incidence rates and rate ratios using SEER*Stat (version 8.4.2, National Cancer Institute, United States) and trends using Joinpoint Regression Program (version 5.0.2, National Cancer Institute, United States).

RESULTS

A total of 4,669 cases of scrotal cancer were diagnosed from 1999 to 2020, with an average of approximately 212 cases annually and an overall incidence rate of 0.20 per 100,000 (Table 1). Incidence rates were highest among men aged 70 years and older (0.82 per 100,000) and 60–69 years (0.40 per 100,000). By race and ethnicity, rates were highest among non-Hispanic Asian or Pacific Islander men (0.31 per 100,000) and were 1.6 (95% CI: 1.4, 1.8) times higher than non-Hispanic White men (0.20 per 100,000). Geographically, incidence rates were higher in the West (0.23 per 100,000) and Northeast (0.21 per 100,000) regions compared to other Census regions. Squamous cell carcinoma (35.9% of all cases) was the most common histology reported, followed by extramammary Paget disease (20.8%), sarcoma (20.5%), and basal cell carcinoma (14.7%). Sensitivity analyses excluding extramammary Paget disease and sarcoma subtypes yielded comparable incidence rates and rate ratios, except for non-Hispanic Black men, who had the highest incidence rate of any race and ethnicity group (Supplementary Table 1).

From 1999 to 2019, scrotal cancer incidence rates were stable overall and in each age group (Table 2). Incidence rates decreased by 2.9% per year from 1999 to 2019 among non-Hispanic Asian or Pacific Islander men but remained stable among other race and ethnicity groups. Rates were stable in all Census regions. Incidence rates of extramammary Paget disease increased by 1.8% per year from 1999 to 2019, while rates of basal cell carcinoma decreased by 8.1% per year from 1999 to 2006. Rates remained stable for all other histologic subtypes.

DISCUSSION

In this analysis of population-based cancer registry data from the United States, the overall annual frequency (212 cases) and incidence rate (0.20 per 100,000) of scrotal cancer was low. However, the overall incidence rate was considerably higher than previously reported from 1973 (0.049 per 100,000) to 2002 (0.095 per 100,000).[2] These higher incidence rates could reflect an increase in detection, partly due to greater awareness of scrotal abnormalities and increased practice of self-examination.[12,13] Our analysis also covered approximately 96% of the United States population, giving us higher case ascertainment and accurately reflecting the underlying incidence rate. The relatively higher case count allowed us to unmask and highlight racial differences in incidence rates by showing that non-Hispanic Asian or Pacific Islander men, who were previously aggregated with different race groups and categorized in the “other” race category,[2] had the highest incidence rate.

In contrast to the 3.2% annual increase in scrotal cancer incidence rate reported from 1973 to 2002 in the United States,[2] overall incidence rates remained stable in our study. Outside the United States, an analysis of the Netherlands Cancer Registry also reported stable scrotal cancer incidence rates from 1989 to 2006 at approximately 0.15 per 100,000.[3] Although overall trends remained stable in our study, rates decreased among non-Hispanic Asian or Pacific Islanders and increased among men with extramammary Paget disease. The reasons for these temporal trends are unclear; however, a study using SEER data also showed an increase in the incidence of extramammary Paget disease, likely due to improvements in disease recognition and diagnosis.[14] Additional studies could elucidate some of these findings since scrotal cancer etiology, pathogenesis, and prognosis vary by tumor histology.[3,15,16]

Similar to previous reports,[2,3] SCC was the most common histologic subtype, accounting for more than one-third of the cases, followed by extramammary Paget disease and sarcoma, each accounting for approximately 20% of subtypes in this study. While still common, the proportion of cases with SCC has declined considerably over the years.[2,3] Changes in the distribution of histologic subtypes may be important to monitor over time as it could have implications for scrotal cancer survival. Analyses of the SEER registry show that overall survival varies by tumor histology and is lower for SCC than other nonsquamous subtypes,[2,15] with a reported difference of 28 months in median survival between patients with SCC and sarcoma.[15] Monitoring trends by histology could also allow us to understand and track the shift in scrotal cancer risk factors, such as the transition from predominantly occupational to non-occupational exposures.[17] For instance, recent research suggests an etiologic role of HPV in the development of SCC.[4–6] The latest World Health Organization

(WHO) 2022 classification series of male genitourinary tumors incorporates scrotal cancers for the first time.[18] The classification of scrotal precursor and invasive lesions follows the schema of penile cancer, which includes classification by HPV-associated and HPV-independent pathways.[19]

Our findings are subject to at least two limitations. First, incidence rates and trends could not be examined by important risk factors, including iatrogenic conditions, HPV infection, and occupational exposures, as these data are not routinely collected by cancer registries. Second, small case counts in some groups, such as histologic subtypes, could lead to unstable trends. However, our data-dependent method for model selection (weighted Bayesian information criterion) is more sensitive to small case counts and effect sizes.[20] Despite limitations, our study used high-quality population-based data to analyze the largest number of scrotal cancer cases in the United States.

CONCLUSION

Scrotal cancer incidence rates were mostly stable during the study period, but the magnitude of rates was higher than previously reported. Continued surveillance and potential linkage of HPV and exposure data with registry data could be valuable in investigating scrotal cancer incidence rates and trends by possible risk factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Age-standardized scrotal cancer incidence rate by select characteristics — United States, 1999–2020

Characteristic	No. of men (%)	Rate[a] (95% CI)	Rate ratio (95% CI)
Total	4,669 (100.0)	0.20 (0.19, 0.21)	—
Age at diagnosis (years)			
18–49	623 (13.3)	0.04 (0.04, 0.05)	Reference
50–59	828 (17.7)	0.20 (0.19, 0.21)	4.5 (4.1, 5.0)
60–69	1,141 (24.4)	0.40 (0.38, 0.42)	8.8 (8.0, 9.7)
>70	2,077 (44.5)	0.82 (0.79, 0.86)	18.2 (16.7, 19.9)
Race and ethnicity [b]			
non-Hispanic White	3,421 (73.3)	0.20 (0.19, 0.20)	Reference
non-Hispanic Black	456 (9.8)	0.19 (0.17, 0.21)	1.0 (0.9, 1.1)
non-Hispanic American Indian or Alaska Native	18 (0.4)	0.12 (0.07, 0.20)	0.6 (0.4, 1.0)
non-Hispanic Asian or Pacific Islander	289 (6.2)	0.31 (0.28, 0.35)	1.6 (1.4, 1.8)
Hispanic	299 (6.4)	0.15 (0.13, 0.17)	0.8 (0.6, 1.0)
Unknown	186 (4.0)	—	—
Census region [c]			
West	1,209 (25.9)	0.23 (0.22, 0.25	Reference
Northeast	975 (20.9)	0.21 (0.20, 0.23)	0.9 (0.8, 1.0)
Midwest	917 (19.6)	0.19 (0.18, 0.20)	0.8 (0.7, 0.9)
South	1,568 (33.6)	0.18 (0.17, 0.19)	0.8 (0.7, 0.8)
Stage [d]			
Early	3,359 (71.9)	0.14 (0.14, 0.15)	—
Late	749 (16.0)	0.03 (0.03, 0.03)	—
Unknown/unstaged	559 (12.0)	0.02 (0.02, 0.03)	—
Histology			
SCC	1,677 (35.9)	0.07 (0.07, 0.07)	—
EMPD	9/0 (20.8)	0.04 (0.04, 0.05)	—
Sarcoma	959 (20.5)	0.04 (0.04, 0.04)	—
BCC	687 (14.7)	0.03 (0.03, 0.03)	—
Adenocarcinoma	167 (3.6)	0.01 (0.01, 0.01)	—
Melanoma	147 (3.1)	0.01 (0.01, 0.01)	—
Other	62 (1.3)	0.00 (0.00, 0.00)	—

Abbreviations: BCC, basal cell carcinoma; CI, confidence interval; EMPD, extramammary Paget disease; SCC, squamous cell carcinoma.

Notes:

[a] Incidence rates are per 100,000.

[b] Hispanic persons might be of any race.

[c] **West:** Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming. **Northeast:** Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. **Midwest:** Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, and Wisconsin. **South:** Alabama, Delaware,

District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia.

[d.] Cancer stage derived using SEER Summary Stage guidelines. Early = localized cancers, Late = regional and distant cancers, and unstaged/unknown.

Table 2.

Trends in age-standardized incidence of scrotal cancer by sociodemographic characteristics — United States, 1999–2019

Characteristic	Years	APC (95% CI)
Overall	1999–2019	0.1 (−0.3, 0.53)
Age at diagnosis (years)		
18–49	1999–2019	−0.4 (−1.6, 0.9)
50–59	1999–2019	0.9 (−0.2, 2.0)
60–69	1999–2019	0.3 (−0.9, 1.5)
>70	1999–2019	−0.2 (−1.1, 0.8)
Race and ethnicity [a]		
non-Hispanic White	1999–2019	0.0 (−0.7, 0.8)
non-Hispanic Black	1999–2019	1.0 (−1.0, 3.5)
non-Hispanic American Indian or Alaska Native	—[b]	—[b]
non-Hispanic Asian or Pacific Islander	1999–2019	−2.9 (−4.5, −1.0)[c]
Hispanic	1999–2019	−1.6 (−4.3, 1.8)
Census region		
West	1999–2019	−0.6 (−1.8, 0.7)
Northeast	1999–2019	0.2 (−0.9, 1.4)
Midwest	1999–2019	−0.1 (−1.5, 1.4)
South	1999–2019	0.7 (−0.2, 1.8)
Histology		
SCC	1999–2019	0.0 (−1.1, 1.3)
EMPD	1999–2019	1.8 (0.6, 3.3)[c]
Sarcoma	1999–2019	0.4 (−1.1, 1.9)
BCC	1999–2006	−8.1 (−14.6, −4.7)[c]
	2006–2019	1.2 (−0.4, 3.7)
Adenocarcinoma	—[b]	—[b]
Melanoma	—[b]	—[b]

Abbreviations: APC, annual percent change; BCC, basal cell carcinoma; CI, confidence interval; EMPD, extramammary Paget disease; SCC, squamous cell carcinoma.

Notes:

[a] Hispanic persons might be of any race.

[b] Trends for counts of fewer than 6 cases were suppressed.

[c] Incidence rate increased or decreased significantly.