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Frequency and distribution of primary site among gender minority cancer patients: An analysis of U.S. national surveillance data

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ABSTRACT

Background: Transgender people and persons with disorders of sex development (DSD) are two separate categories of gender minorities, each characterized by unique cancer risk factors. Although cancer registry data typically include only two categories of sex, registrars have the option of indicating that a patient is transgender or has a DSD.

Methods: Data for primary cancer cases in 46 states and the District of Columbia were obtained from the North American Association of Central Cancer Registries (NAACCR) database for the period 1995–2013. The distributions of primary sites and categories of cancers with shared risk factors were examined separately for transgender and DSD patients and compared to the corresponding distributions in male and female cancer patients. Proportional incidence ratios were calculated by dividing the number of observed cases by the number of expected cases. Expected cases were calculated based on the age- and year of diagnosis-specific proportions of cases in each cancer category observed among male and female patients.

Results: Transgender patients have significantly elevated proportional incidence ratios (95% confidence intervals) for viral infection induced cancers compared to either males (2.3; 2.0–2.7) or females (3.3; 2.8–3.7). Adult DSD cancer patients have a similar distribution of primary sites compared to male or female patients but DSD children with cancer have ten times more cases of testicular malignancies than expected (95% confidence interval: 4.7–20).

Conclusion: The proportions of certain primary sites and categories of malignancies among transgender and DSD cancer patients are different from the proportions observed for male or female patients.

1. Introduction

Population-based cancer registries are important in assessing trends in cancer frequency, distribution, and survival [1]. Although reports using registry data typically include only two categories of sex, some groups of people cannot be explicitly categorized as “male” or “female.” Transgender people and persons with disorders of sex development (DSD) represent two such distinct groups with unique medical treatments and cancer risk factors [2].

Transgender people comprise a diverse group of individuals whose biological sex does not match their gender identity [3]. Gender identity can be defined as one’s sense of being a boy/man, girl/woman, neither or both [4]. Although cancer risk in this population is not well understood, it remains an important area of concern [5,6] because transgender people have higher prevalence of established cancer risk factors such as sexually transmitted infections and lack of screening [7]. In addition, transgender people who undergo gender affirmation treatment may receive high doses of sex steroid hormones for extended periods of time; the carcinogenicity of hormone therapy in this context is also unclear [8,9].

The term DSD refers to a heterogeneous group of conditions affecting the development of sex chromosomes, gonads, or anatomic sex [10,11]. DSD can be identified at birth by the presence of atypical genitalia, during adolescence by the absence of or contra-sexual pubertal development, or in adulthood following discovery of fertility problems. Patients with DSD may be at higher risk for gonadal

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malignancies depending on the specific condition [12–14]. For example, DSD patients who have Y chromosome material may have an increased risk of germ cell tumors [15–17].

Transgender people and persons with DSD are often included in the broad and heterogeneous category of sexual and gender minorities. Sexual minorities are defined as individuals who identify as lesbian, gay, or bisexual or report same-sex attraction [18]. By contrast, transgender people and persons with DSD are usually described as gender minorities, although an argument can be made that DSD may or may not belong in this group [2].

Data on cancer cases in all 50 states and the District of Columbia are collected by the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. These data are compiled by the North American Association of Central Cancer Registries (NAACCR); access to the NAACCR database offers opportunities for analyses of cancer patterns and trends within the entire United States population [19]. In collecting information for the variable 'sex', registrars have always had the option of selecting one of the mutually exclusive categories of "male," "female," "transsexual" and "other (hermaphrodite)," based on information in the medical records, which may be self-reported or indicated by a healthcare provider [20]. Although inaccurate, the term 'hermaphrodite' has historically been used to refer to people with DSD [21].

To-date these data have not been examined on a national scale. For this reason, the objectives of this study were to examine the distributions of primary sites and categories of malignancies among transgender and DSD cancer patients reported to NAACCR and compare these distributions to those observed among patients characterized as "male" or "female."

2. Methods

Demographic and tumor information for all first primary cancer cases diagnosed from 1995 through 2013 was extracted from the NAACCR Cancer in North America (CiNA) Deluxe database for the 46 participating states and the District of Columbia for all years with available data [22]. As categories of gender beyond male and female are not traditionally released with CiNA data, a consent process was required from each individual state to access the full set of codes for the variable "sex." Four states did not provide consent to use these data and were not included in analyses. Gender was categorized as male, female, transgender, or DSD based on the NAACCR variable "sex."

Patients were also characterized by year of diagnosis, age at diagnosis, race/ethnicity, region of diagnosis, insurance status, and primary site of cancer. Year of diagnosis was categorized into 5-year groups, age was categorized into 10-year groups, and region of diagnosis was categorized according to the U.S. Census Bureau designation as: Northeast (CT, ME, MA, NH, RI, NJ, NY, PA), Midwest (IN, MI, OH, WI, IA, MO, NE, ND, SD), South (DE, D.C., FL, GA, MD, NC, SC, VA, WV, AL, KY, MS, TN, AR, LA, OK, TX), and West (AZ, CO, ID, NM, MT, UT, NV, WY, AK, CA, HI, OR, WA).

To compare the distributions of cancer sites and categories of malignancies among transgender and DSD patients to that observed among male and female patients, the proportional incidence ratios (PIR) and corresponding Poisson distribution-based 95% confidence intervals (95% CI) were calculated for the primary sites with greater than five cases and for groups of cancers with shared risk factors. Cancers were grouped as any viral infection induced cancers, AIDS-defining cancers, HPV-related cancers, and smoking-related cancers. PIR was calculated by dividing the number of observed cases by the number of expected cases. Expected cases were calculated based on the proportion of cases for each primary site or category among all cancers reported for males and females, separately, within age- and year of diagnosis- specific strata. PIR was restricted to patients ≥20 years old at diagnosis because very few cases were reported among transgender and DSD patients in younger age groups. The only exception was made for testicular cancers in DSD patients because of the reported increased risk of pediatric germ cell tumors in this group [23]. In this case, PIR was calculated separately for patients 0–19 years old within 10-year age- and year of diagnosis- specific strata. Statistical analysis was conducted using SAS 9.4.

3. Results

A total of 1223 cases diagnosed between 1995 and 2013 in the NAACCR database had a value for the "sex" variable other than "male" or "female." Two-thirds (n = 805) were transgender and one-third (n = 418) were DSD patients (Table 1). A total of 21,824,591 primary cancer cases diagnosed in the U.S. during the same period were characterized as either "male" or "female." The number of patients recorded as either transgender or DSD increased over time and was greatest in the most recent time period (2010–2013). This secular trend was not observed for male or female patients. Compared to male and female patients, transgender and DSD patients were more likely to be diagnosed at younger ages. A greater proportion of the DSD patients were diagnosed as children or adolescents than transgender patients (2.6% vs. 0.7%) and the percentage of DSD patients younger than 30 years old at diagnosis was nearly double the corresponding percentage of male and female referents; however the majority of DSD cancer patients were still diagnosed at more advanced age. The race/ethnicity distributions were similar for males and females, but transgender and DSD patients included greater proportions of minorities (29–30%). Similar to male and female patients, the greatest proportion of DSD patients resided in the South, whereas transgender patients were more likely to be located in the West (41%). Transgender patients were also more likely to be Medicaid-insured or uninsured, while nearly one-third of DSD patients had Medicare.

The frequencies and distributions of primary cancer sites among adult transgender patients are presented in Table 2. The most common cancer sites were lung/bronchus (95 cases), colorectum (86 cases), non-Hodgkin lymphoma (65 cases), prostate (48 cases), and breast (43 cases). The highest PIRs were observed for anal (9.5; 95% CI: 6.6–13) and breast (21; 15–28) cancers compared to males, for anal (9.5; 6.7–13) and base of tongue/tonsillar (7.6; 4.4–12) cancers compared to females, and for Kaposi sarcoma compared to either sex (vs. males: 9.2; 6.6–13; vs. females 236; 169–320). Significantly lower PIRs were observed for melanoma (0.5; 0.4–0.8), prostate (0.3; 0.2–0.4), and testicular (0.3; 0.1–0.6) cancers compared to males, and for breast (0.2; 0.1–0.2), cervical (0.3; 0.1–0.6), ovarian (0.4; 0.2–0.8), and thyroid (0.3; 0.2–0.5) cancers compared to females.

Table 3 presents the frequency and PIR (95% CI) results for DSD patients. One-quarter of the cases (n = 101) were cancers of the breast. The other most common sites were colorectum (48 cases), lung/bronchus (48 cases), melanoma (28 cases), and prostate (19 cases). A significantly elevated PIR among DSD patients was observed for breast cancer (101; 82–123) compared to males. The PIR for testicular cancer comparing DSD adults to adult males was not elevated; however, the corresponding PIR for DSD children 0–19 years of age was significantly higher than expected (10; 4.7–20). The majority (82%) of childhood cancers in DSD patients were found in the testis. Significantly lower PIRs were observed for prostate (0.2; 0.1–0.3) and urinary bladder (0.4;