Cancer Epidemiology 55 (2018) 68–72

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Testicular cancer among US men aged 50 years and older

Armen A. Ghazarian[a,b,1], Carsten Rusner[c,1], Britton Trabert[a], Megan Braunlin[a], Katherine A. McGlynn[a,*], Andreas Stang[d,e,f]

[a] Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA
[b] Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA
[c] Department of Radiology, St. Elisabeth and St. Barbara Hospital, Halle (Saale), Germany
[d] Center of Clinical Epidemiology, Institute of Medical Informatics, Biometry and Epidemiology, University Hospital Essen, Essen, Germany
[e] Department of Epidemiology, School of Public Health, Boston University, Boston, MA, USA
[f] German Consortium of Translational Cancer Research (DKTK), Partner Site University Hospital of Essen, University of Duisburg-Essen, Essen, Germany

ARTICLE INFO

Keywords:
Testicular cancer
TGCT
Trends
NAACCR
Incidence

ABSTRACT

Background: The incidence of testicular cancer in the United States (US) has substantially increased in recent decades. The majority of testicular cancers are germ cell tumors (TGCT), which are the most commonly occurring malignancies among men aged 15–44 years in the US. To date, few studies have focused on testicular cancer among men aged ≥ 50 years. Thus, we sought to examine detailed descriptive features, including incidence rates and age patterns, of tumors that arise in the testes among men aged ≥ 50 years.

Methods: Data from forty-one US cancer registries were included for the years 1999–2014. Incidence rates per 100,000 person-years and their 95% confidence intervals (CI) were calculated by race/ethnicity, histology, and age at diagnosis. Estimates of annual percent change (APC) were also calculated.

Results: Age-specific incidence rates of spermatocytic tumors, sex cord stromal tumors and lymphomas rose with age, while age-specific incidence rates of seminomas and nonseminomas declined. Between 1999 and 2014, the incidence of nonseminoma (APC = 3.26, 95% CI: 2.27–4.25) increased more than any other tumor type. The incidence of seminoma (APC: 1.15, 95% CI: 0.59–1.71) also increased, while rates of testicular lymphoma (APC: −0.66, 95% CI: −1.16 to −0.16), spermatocytic tumors (APC: 0.42, 95% CI: −1.42 to 2.29), and sex cord stromal tumors (APC: 0.60, 95% CI: −3.21 to 4.55) remained relatively unchanged.

Conclusion: Given the distinct time-trends and age-specific patterns of testicular cancer in men aged ≥50 years, additional investigation of risk factors for these tumors is warranted.

1. Introduction

Testicular cancers are rare cancers in the general population, but are the most commonly occurring cancer among men aged 15 to 44 years in the United States [1]. The majority (approximately 98%) of testicular cancers are germ cell tumors (TGCT). TGCTs are classified into three histologic subtypes: seminomas, nonseminomas, and spermatocytic tumors. The median age of diagnosis for seminomas is 35 years and for nonseminomas 25 years while spermatocytic tumors, which are less aggressive and etiologically distinct from seminomas and nonseminomas, peak at an older age (median age 62 years). Seminomas and nonseminomas comprise the majority of germ cell tumors (approximately 56% for seminoma and 43% for nonseminoma) while spermatocytic tumors are much less common, accounting for less than 1% of the total. The small percentage of testicular cancers that are not germ cell tumors (approximately 2%) include sex cord stromal tumors, such as Leydig cell and Sertoli cell tumors, as well as other rare or poorly defined histologic subtypes.

The incidence of TGCT has substantially increased in recent decades [2]. The rapid increase in incidence suggests that critical changes in environmental factors may contribute to the development of TGCT [3]. To date, there are few studies focusing on testicular cancer in men aged ≥ 50 years [4,5]. Thus, the aim of this study was to provide detailed descriptive features, including age patterns and incidence rates of TGCT among men aged ≥ 50 years. In addition to TGCT, we were also interested in other tumors that arise in the testes, such as primary testicular lymphoma; predominantly a disease of men ≥ 50 years and often disregarded in population-based studies.

* Corresponding author at: National Cancer Institute, 9609 Medical Center Drive, Room 6E-446, Bethesda, MD, 20892, USA.
E-mail addresses: mcglynnk@mail.nih.gov, mcglynnk@nih.gov (K.A. McGlynn).
[1] These authors contributed jointly to the manuscript.

https://doi.org/10.1016/j.canep.2018.05.007
Received 22 March 2018; Received in revised form 15 May 2018; Accepted 16 May 2018

2. Methods

Primary malignant testicular cancers were identified from the Cancer Incidence in North America (CiNA) analytic file provided by the North American Association of Central Cancer Registries (NAACCR). Cancer incidence data that meet high-quality standards from the SEER program and the Centers for Disease Control and Prevention's National Program of Cancer Registries are included in the CiNA analytic data set [6]. Data from forty-one registries were included for the years 1999 through 2014. These registries included Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming (approximately 90% coverage of the US population). The CiNA analytic file dates back to 1995, but due to missing data from many of the registries, we restricted all analyses to the year 1999 forward.

Testicular cancers were defined using the International Classification of Diseases for Oncology (3rd ed.) topography (C62) and morphology codes (germ cell tumors: 9060/3–9062/3, 9064/3–9102/3; seminoma: 9060/3–9062/3, 9064/3; nonseminoma: 9065/3-9102/3; spermatocytic tumors: 9063/3; sex cord stromal tumors: 8640/3, 8650/3) [7]. Nonseminomas were further classified as: embryonal carcinoma (9070/3, 9072/3), yolk sac tumors (9071/3), teratoma (9080/3, 9082–9084/3, 9102/3), choriocarcinoma (9100/3, 9101/3), and mixed germ cell tumors (9081/3, 9085/3). Primary testicular lymphomas were identified using a combination of topography (C62) and morphology codes for lymphoma. Incidence rates per 100,000 person-years, age-adjusted to the US 2000 standard population, and their 95% confidence intervals were calculated. Testicular cancer incidence rates were calculated by histologic subtype and age of diagnosis. Estimates of annual percent change (APC) were calculated for the 1999–2014 time period using the annual rates and weighted least squares regression [8]. For temporal analysis, years of diagnosis were grouped into four periods: 1999–2002, 2003–2006, 2007–2010, and 2011–2014. Age of diagnosis was grouped into 8 categories: 50–54 years, 55–59 years, 60–64 years, 65–69 years, 70–74 years, 75–79 years, 80–84 years, and 85+ years. All statistical analyses were performed using the SEER*Stat statistical package (version 8.3.4).

3. Results

Between 1999–2014, 9353 seminomas, 2227 nonseminomas, 533 spermatocytic tumors, 4534 testicular lymphomas, and 288 sex cord stromal tumors were diagnosed among residents of the 41 SEER/NPCR registry areas (Table 1). The percent of tumors that were histologically verified was 99% for all TGCTs (seminomas, nonseminoma, spermatocytic tumors), 97% for testicular lymphomas, and 99% for sex cord stromal tumors.

Of all the tumors, the incidence of nonseminoma increased most notably (APC = 3.26, 95% CI: 2.27–4.25) (Table 1, Fig. 1A). Among nonseminomas, the greatest increase in incidence rates was among mixed germ cell tumors (APC: 4.38, 95% CI: 3.03–5.75) (Table 1). Incidence rates of seminoma also increased (APC: 1.15, 95% CI: 0.59–1.71), while rates of testicular lymphoma (APC: -0.66, 95% CI: −1.16 to −0.16), spermatocytic tumors (APC: 0.42, 95% CI: −1.42 to 2.29), and sex cord stromal tumors (APC: 0.60, 95% CI: −3.21 to 4.55) remained relatively unchanged throughout the time period (Table 1, Fig. 1A).

Incidence rates of testicular cancer by histologic subtype and age of diagnosis are presented in Supplementary Table 1 and Fig. 1B. The incidence of testicular lymphoma increased from age 50 to age 80–84 years. Among men aged ≥ 70 years, lymphoma was the most commonly occurring cancer in the testis. In contrast, rates of seminoma and nonseminoma declined steadily from the age of 50 years, while the incidence of spermatocytic tumors and sex cord stromal tumors increased steadily. At no age, however, was the incidence of spermatocytic tumors higher than the incidence of seminoma. Sex cord stromal tumors were the most uncommon tumor type at all ages.

Table 1
Age-standardized incidence rates of testicular cancer by histologic subtype among men aged ≥ 50 years, SEER/NPCR Registries, 1999–2014.

	Count	Rate (95% CI)[a]	APC (95% CI)
Seminoma	9353	1.46 (1.43–1.49)	1.15 (0.59–1.71)
Nonseminoma	2227	0.35 (0.33–0.36)	3.26 (2.27–4.25)
Embryonal carcinoma	426	0.07 (0.06–0.07)	−0.24 (−2.17 to 1.72)
Yolk sac tumors	92	0.01 (0.01–0.02)	[b]
Teratoma	87	0.01 (0.01–0.02)	2.25 (−1.64 to 6.29)
Choriocarcinoma	131	0.02 (0.02–0.02)	0.29 (−3.34 to 4.06)
Mixed germ cell tumors	1,339	0.21 (0.20–0.22)	4.38 (3.03–5.75)
Spermatocytic tumors	533	0.09 (0.09–0.10)	0.42 (−1.42 to 2.29)
Testicular lymphomas	4534	0.75 (0.72–0.77)	−0.66 (−1.16 to −0.16)
Sex cord stromal tumors	288	0.05 (0.04–0.05)	0.60 (−3.21 to 4.55)

APC = Annual Percent Change.
CI = Confidence Interval.
[a] Rates are per 100,000 and age-adjusted to the 2000 US Standard Population.
[b] The APC could not be calculated.

Incidence rates of testicular cancer by race/ethnicity are presented in Table 2. Non-Hispanic white men had the highest rates of TGCT overall (rate: 2.14, 95% CI: 2.10–2.18), followed by Hispanic (rate: 0.98, 95% CI: 0.89–1.07), Asian/Pacific Islander (rate: 0.60, 95% CI: 0.51–0.70), and non-Hispanic black men (rate: 0.50, 95% CI: 0.44–0.56). The same rankings were similar for all TGCT histological subtypes (seminoma, nonseminoma, spermatocytic tumors) with higher rates among Non-Hispanic whites and Hipanics than among Non-Hispanic blacks and Asian/Pacific Islanders. The incidence of testicular lymphomas was also highest among non-Hispanic white men (rate: 0.80, 95% CI: 0.77–0.82), followed by Asian/Pacific Islander (rate: 0.72, 95% CI: 0.62–0.84), Hispanic (rate: 0.71, 95% CI: 0.63–0.80), and non-Hispanic black men (rate: 0.24, 95% CI: 0.20–0.29). Among sex cord stromal tumors, the incidence was highest among non-Hispanic black men (rate: 0.07, 95% CI: 0.05–0.10), followed by non-Hispanic white (rate: 0.05, 95% CI: 0.04–0.05), Hispanic (rate: 0.04, 95% CI: 0.03–0.07), and Asian/Pacific Islander men (rate: 0.01, 95% CI: 0.01–0.06).

4. Discussion

During the time period 1999–2014, incidence rates of nonseminoma among men of ages 50 and greater, increased more notably than incidence rates of other tumors arising in the testis. Incidence rates of seminoma also increased, while rates of spermatocytic tumors, testicular lymphomas, and sex cord stromal tumors remained relatively unchanged throughout the time period. The examination of age-specific rates revealed that the incidence of spermatocytic tumors, sex cord stromal tumors, and testicular lymphoma increased steadily with age in contrast to rates of seminoma and nonseminoma, which steadily declined with age.

The current study found that testicular lymphoma is the most commonly occurring testicular malignancy among men aged ≥ 70 years. Primary testicular lymphoma is a rare, clinically aggressive form of extranodal non-Hodgkin lymphoma (NHL) accounting for < 5% of testicular cancers. The vast majority of cases are classified as histologically diffuse large B-cell lymphoma with high bilateral testicular involvement. There are limited data regarding specific risk factors for testicular lymphoma, however, human immunodeficiency virus (HIV)