

Trends in Testicular Germ Cell Tumors Among U.S. Military Servicemen, 1990–2003

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ABSTRACT Objective: To determine the incidence of testicular germ cell tumors among active duty males and compare it with the incidence in the general U.S. population. Methods: The Automated Cancer Tumor Registry and the Surveillance, Epidemiology, and End Results Program data from 1990 to 2003 were analyzed for men aged between 20 and 59 years by histology and stage at diagnosis. Rates were age adjusted using the male active duty military population as the standard. Results: Nonseminoma incidence was significantly lower in the military than in the general population (incidence rate ratio = 0.90, 95% confidence interval = 0.82–0.98). Trends in incidence tended to be similar in both the populations. Increases were observed for both histologic types but were only significant for seminoma (Automated Cancer Tumor Registry: 21% and Surveillance, Epidemiology, and End Results program: 16%; $p < 0.05$). Increases in incidence were only observed for localized tumors of both histologic types. Conclusions: The lower incidence of nonseminoma in the military and the increased incidence of localized tumors in both populations remain unexplained.

INTRODUCTION

Testicular germ cell tumors (TGCT) are the most commonly diagnosed malignancy among young men in the United States and have been increasing for the past several decades.¹ Incidence rates are higher among white men than among men of other racial/ethnic groups.² Two major histologic types of TGCT that occur in young men between the ages of 20 and 40 years are seminomas and nonseminomas. A third type of TGCT, spermatocytic seminoma, is rare overall and has an older peak age at incidence of 50 to 55 years. An examination of national trends has reported a more pronounced increase in the incidence of seminoma than nonseminoma and more notable increases for early-stage tumors of both histologic types.²

TGCT among active duty military men is an important health outcome, given that it occurs at a young age. The etiology of TGCT is still poorly understood; the only major, well-established risk factors are cryptorchidism and prior personal

or family history of TGCT.³ Studying incidence trends among men in the military, who may have different exposures than men in the general population, may provide helpful insight into the etiology of TGCT.

Although the overall incidence of TGCT in the military has increased in a similar manner to that in the general population,^{4,5} in contrast to the national trends,² a study conducted among a predominantly (92.3%) white population at one military medical center indicated that the proportion of TGCT that were nonseminomas rose, whereas the proportion of seminomas decreased between 1988 and 2007.⁶ It is unclear, however, if these trends by histology were unique to this particular medical center or to the military in general. Therefore, the aim of this study was to further compare among active duty servicemen and men in the general U.S. population the incidence of TGCT by race, histology, and stage at diagnosis, over time.

MATERIALS AND METHODS

TGCT incidence data, excluding spermatocytic seminoma, among active duty servicemen aged between 20 and 59 years were obtained from the U.S. military's Automated Cancer Tumor Registry (ACTUR). ACTUR was established in 1986 and is the data collection and clinical tracking system for all cancer cases diagnosed or treated at military treatment facilities among Department of Defense beneficiaries. For the purposes of this study, data were included for cases diagnosed from 1990 to 2003. Although all data submitted to ACTUR are reviewed and verified for accurate diagnoses, data before 1990 were not included to minimize the possibility of incomplete recording. Additionally, although ACTUR includes data for more recent years, this information was not available to us for analyses. Procedures, which have been previously described,⁵ were developed using national and state cancer registry guidelines^{7,8} to identify and consolidate duplicate records so that only one record existed for each primary cancer. Stage at diagnosis (localized,

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We certify that all individuals who qualify as authors have been listed; that each has participated in the conception and design of this work, the analysis of data (when applicable), the writing of the document, and the approval of the submission of this version; that the document represents valid work; that if we used information derived from another source, we obtained all necessary approvals to use it and made appropriate acknowledgements in the document; and that each takes public responsibility for it. Nothing in the presentation implies any Federal/Department of Defense/Department of Defense endorsement. The opinions and assertions contained herein are the private views of the authors and do not reflect the official views of the U.S. Departments of the Army, Navy, or Defense, National Cancer Institute, or U.S. Government.

non-localized: regional/distant) was determined by combining two variables: "SEER Summary Stage 1977" (diagnosis years: 1990–2000) and "SEER Summary Stage 2000" (diagnosis years: 2001–2003). When there were multiple records per tumor at the time of diagnosis and the tumor stage codes differed, determination of stage was based on surgery records if available. If no surgery records were available, the most advanced stage noted was selected. The annual population counts of active duty male military personnel were obtained from the Defense Manpower Data Center, which maintains demographic and military data on personnel in all military services.

TGCT incidence data among males aged between 20 and 59 years in the general U.S. population were obtained from the Surveillance, Epidemiology, and End Results (SEER) program. SEER, sponsored by the National Cancer Institute (NCI), began consolidating data from U.S. cancer registries in 1973. TGCT and population counts from 1990 to 2003 were obtained from the original 9 SEER registries: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle–Puget Sound, and Utah.⁹ These registries represent approximately 10% of the U.S. population. Stage at diagnosis (localized, non-localized: regional/distant) was determined according to "SEER Historic Stage A."

TGCT was defined using the International Classification of Disease for Oncology topographic (C62) and morphologic codes (seminoma: 9060-9062, 9064; nonseminoma: 9065-9101). Demographic and tumor characteristics were obtained for each case. The analysis was restricted to white and black men because military denominator data were only available for these racial categories. For trend analysis, years of diagnosis were grouped into three categories: 1990–1994, 1995–1999, and 2000–2003. Temporal trends were plotted with the use of semilogarithmic scales so that slopes or rates of change could be compared.¹⁰ Age-adjusted incidence rates, incidence rate ratios (IRRs), and their 95% confidence intervals (CIs) were calculated using the Tiwari method.¹¹ All incidence rates were age adjusted to the combined active duty military population from 1990 to 2003 using four 10-year age groups (20–59 years) and were expressed per 100,000 man-years. The significance level was specified as $p < 0.05$. All calculations were done using SAS statistical software, version 9.1 (SAS Institute, Cary, North Carolina).¹¹

This study utilized de-identified data and was approved by the Institutional Review Boards of U.S. Military Cancer

Institute, Armed Forces Institute of Pathology, and National Cancer Institute, National Institutes of Health.

RESULTS

Age-adjusted incidence rates of seminoma and nonseminoma among white and black military servicemen (ACTUR data) and men in the general population (SEER data) for the 14-year time period 1990–2003 are presented in Table I. In both populations, seminoma rates were higher than nonseminoma rates and rates of both histologic types were higher among white men than black men. In comparing the two populations, the incidence of seminoma in the military was not significantly different from that in the general population among either white or black men (white: IRR = 1.02, 95% CI = 0.94–1.10; black: IRR = 1.12, 95% CI = 0.76–1.60). The incidence of nonseminoma, however, was significantly lower in the military among both white and black men (white: IRR = 0.90, 95% CI = 0.82–0.98; black: IRR = 0.47, 95% CI = 0.23–0.86).

Given the small number of total TGCTs among black men, further stratification by histologic type and year of diagnosis and stage was not possible; 42 (89%) of the seminomas and 10 (77%) of the nonseminomas among blacks were localized tumors. As a result, the subsequent analyses were limited to white men. Over time, seminoma and nonseminoma rates rose in both ACTUR and SEER but only the increases in seminoma were statistically significant (Fig. 1; Table II). Seminoma rates rose 21% in the military and 16% in the general population between 1990–1994 and 2000–2003 ($p < 0.05$). Rates of localized seminoma tumors increased significantly in both the military and general population (38% and 22%, respectively), whereas those for non-localized seminoma declined 51% in the military but were stable in the general population.

The incidence of localized nonseminoma increased significantly, i.e., 46% in the military and 16% in the general population ($p < 0.05$). The declines in non-localized nonseminoma of 8% in the military and 13% in the general population were not statistically significant.

Among both the military and general population, localized seminoma rates were four to six times greater than the rates of non-localized seminoma. In contrast, about half of the nonseminomas were diagnosed at a localized stage and half at a non-localized stage. No great difference in incidence by service branch were evident (Table III).

TABLE I. TGCT Incidence in the U.S. Active Duty Military Population (ACTUR) and the General Population (SEER) Among Men Aged 20–59 Years by Race and Histologic Type, 1990–2003

Race	Histologic Type	ACTUR			SEER			ACTUR:SEER	
		Count	Rate ^a	95% CI	Count	Rate ^a	95% CI	IRR	95% CI
White	Seminoma	882	6.71	6.28–7.17	5,207	6.60	6.39–6.82	1.02	0.94–1.10
	Nonseminoma	726	5.57	5.17–5.99	3,238	6.21	5.96–6.45	0.90	0.82–0.98
Black	Seminoma	47	1.39	1.02–1.85	141	1.24	1.01–1.50	1.12	0.76–1.60
	Nonseminoma	13	0.39	0.21–0.67	68	0.83	0.63–1.07	0.47	0.23–0.86

^aRates are per 100,000 person-years and age adjusted to the combined 1990–2003 active duty military population using four 10-year age groups.

DISCUSSION

In comparison to the general population, the incidence of nonseminoma was significantly lower in the military between 1990 and 2003. Temporal trends in incidence by histology and stage at diagnosis, however, tended to be similar between the

two populations. Incidence rates increased for both histologic types of TGCT, but were significant only for seminoma. When stratified by stage at diagnosis, significant increases in incidence were observed for localized tumors regardless of histologic type.

The etiology of TGCT is poorly understood. The only established risk factors are cryptorchidism and prior diagnosis of TGCT or family history of TGCT.³ It is not clear whether seminoma and nonseminoma have divergent risk patterns. As a consequence, the reasons for the lower incidence of nonseminoma in the military are not certain. It is possible, however, that rates of nonseminoma are lower in the military population because the peak age at diagnosis of nonseminoma is quite young. Forty-six percent of nonseminomas in the general population occur among men in their 20s.¹² In contrast, only 22% of seminomas occur among men in their 20s.¹² Therefore, young men who have symptoms of nonseminoma might be less likely to attempt to enlist in the military than men who are not having any symptoms. It is also possible that physical examinations before enlistment may detect nonseminomas.

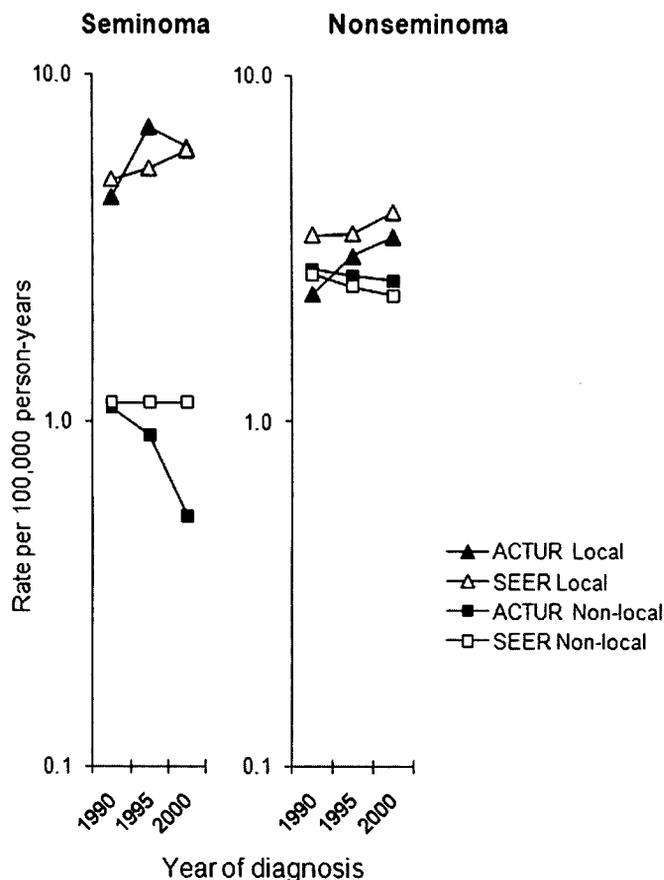


FIGURE 1. Trends in testicular cancer incidence among white men in ACTUR and SEER-9 diagnosed from 1990–1994 to 2000–2003 by histologic type and stage. Rates are age adjusted to the combined 1990–2003 active duty military population using four 10-year age groups, and each point represents 4 or 5 years.

TABLE III. TGCT Incidence in the U.S. Active Duty Military Population (ACTUR) Among White Men Aged 20–59 Years by Histologic Type and Service Branch, 1990–2003

Histologic Type	Service Branch	Count ^a	Rate ^b	95% CI
Seminoma	Army	254	6.70	5.90–7.57
	Navy	256	6.86	6.05–7.76
	Air Force	279	6.98	6.17–7.86
	Marines	69	5.93	4.56–7.59
	Coast Guard	22	5.68	3.52–8.62
Nonseminoma	Army	226	5.80	5.07–6.61
	Navy	196	5.29	4.58–6.09
	Air Force	202	5.93	5.12–6.82
	Marines	78	4.57	3.54–5.83
	Coast Guard	24	6.82	4.34–10.17

^aTwo seminoma cases were not included because the listed service branch was “other.” ^bRates are per 100,000 person-years and age adjusted to the combined 1990–2003 active duty military population using four 10-year age groups.

TABLE II. TGCT Incidence in the U.S. Active Duty Military Population (ACTUR) and the General Population (SEER) by Histologic Type and Tumor Stage Among White Men Aged 20–59 Years, 1990–2003

Histologic Type	Source	Stage	1990–1994			2000–2003			IRR ^b	95% CI
			Count	Rate ^a	95% CI	Count	Rate ^a	95% CI		
Seminoma	ACTUR	All	317	5.62	5.02–6.28	213	6.78	5.90–7.76	1.21	1.01–1.44
		Local	250	4.43	3.90–5.01	192	6.12	5.28–7.05	1.38	1.13–1.67
		Non-local	61	1.09	0.83–1.39	17	0.53	0.31–0.86	0.49	0.27–0.85
SEER	All	1,718	6.18	5.85–6.53	1,628	7.19	6.77–7.63	1.16	1.07–1.26	
	Local	1,350	4.95	4.64–5.26	1,331	6.02	5.63–6.43	1.22	1.11–1.33	
	Non-local	342	1.13	1.00–1.28	288	1.13	0.97–1.30	1.00	0.82–1.21	
Nonseminoma	ACTUR	All	298	5.24	4.66–5.87	186	6.03	5.20–6.97	1.15	0.95–1.39
		Local	133	2.33	1.95–2.77	105	3.42	2.79–4.14	1.46	1.12–1.91
		Non-local	157	2.76	2.35–3.23	79	2.55	2.02–3.18	0.92	0.69–1.22
SEER	All	1,150	6.22	5.82–6.64	954	6.41	5.95–6.89	1.03	0.93–1.14	
	Local	639	3.45	3.16–3.77	590	4.01	3.65–4.40	1.16	1.02–1.32	
	Non-local	491	2.66	2.40–2.94	355	2.31	2.04–2.60	0.87	0.74–1.02	

^aRates are per 100,000 person-years and age adjusted to the combined 1990–2003 active duty military population using four 10-year age groups. ^bIncidence rate ratio comparing 2000–2003 to 1990–1994. The sum of the local and non-local tumors is less than the total (all) because the total includes unstaged tumors.

The observed greater increase in incidence of seminoma than nonseminoma, especially localized seminoma, was in agreement with previous national studies.^{2,13,14} However, the difference in trend by histologic type among men in the military was less pronounced. Additionally, in contrast to a previous study⁶ conducted at one military medical center, military-wide findings of the current study indicated that the proportion of TGCT that was seminoma increased slightly between 1990 and 2003. In the previous study, seminomas comprised 54% of TGCTs in 1988–1997, which decreased to 44% in 1998–2007, whereas the findings of the current study indicate that seminomas comprised 52% of the TGCTs in 1990–1994 and 53% in 2000–2003. The inconsistencies between these two studies may have resulted from differences in study populations, although age at diagnosis was very similar in the two studies; 28.9 years in the previous study and 29.8 years in the current study. Other differences, such as years of diagnoses, referral patterns, and/or other characteristics of the patient population, however, may account for the discrepancy.

The reasons for the increases in incidence of both localized seminoma and localized nonseminoma are unclear. An increase in localized tumors concurrent with a decrease in non-localized tumors is consistent with a pattern seen with introduction of cancer screening. There is no screening for testicular cancer, however, so a shift toward localized tumors cannot be due to screening. It is possible, of course, that a greater awareness of testicular cancer has developed among young men over time, though evidence of such a change has not been documented. It is also possible that changes in the prevalence of factors specifically associated with local versus non-local (i.e., more aggressive) TGCT have occurred, though what the factors might be remains unclear.

This study had notable strengths in that it examined TGCT rates across all military branches and all medical facilities. However, there is the possibility of under-reporting in ACTUR. Although Department of Defense policies require all cancers to be reported to ACTUR, some military treatment facilities do not have American College of Surgeons approved cancer programs or dedicated registrars. Additionally, any diagnosis and treatment of TGCT among servicemen that was done solely at non-military medical centers would not be captured in ACTUR. Caution must also be exercised when considering the current results as the number of TGCTs included in some of the stratified analyses was not great.

In agreement with previous findings in other populations, the incidence of localized TGCT significantly increased among white men in the U.S. military between 1990 and 2003. Further insight into the etiology of TGCT may be gained by conducting more in-depth studies among military servicemen.

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REFERENCES

1. Horner MJ, Ries LAG, Krapcho M, et al: SEER cancer statistics review, 1975–2006. Bethesda, MD, National Cancer Institute, 2009. Available at http://seer.cancer.gov/csr/1975_2006/, based on November 2008 SEER data submission, posted to the SEER web site; accessed November 2009.
2. Shah MN, Devesa SS, Zhu K, McGlynn KA: Trends in testicular germ cell tumours by ethnic group in the United States. *Int J Androl* 2007; 30: 206–13; discussion 213–4.
3. McGlynn KA: Environmental and host factors in testicular germ cell tumors. *Cancer Invest* 2001; 19: 842–53.
4. Thompson IM, Optenberg S, Byers R, Dove M: Increased incidence of testicular cancer in active duty members of the Department of Defense. *Urology* 1999; 53: 806–7.
5. Zhu K, Devesa SS, Wu H, et al: Cancer incidence in the U.S. military population: comparison with rates from the SEER program. *Cancer Epidemiol Biomarkers Prev* 2009; 18: 1740–5.
6. Cooper DE, L'Esperance JO, Christman MS, Auge BK: Testis cancer: a 20-year epidemiological review of the experience at a regional military medical facility. *J Urol* 2008; 180: 577–81; discussion 581–2.
7. Johnson CH, Peace S, Adamo P, Fritz A, Percy-Laury A, Edwards BK: The 2007 Multiple Primary and Histology Coding Rules. Surveillance, Epidemiology and End Results Program, National Cancer Institute, Bethesda, MD, 2007.
8. The North American Association of Central Cancer Registries: Report of the Automated Tumor Linkage Work Group of the ROC, October 2005. Available at <http://www.naacr.org/StandardsandRegistryOperations/ATLGDocs.aspx>; accessed December 2009.
9. Surveillance Epidemiology and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Incidence—SEER 9 Regs Limited-Use, November 2007 Sub (1973–2005) <Katrina/Rita Population Adjustment>—Linked To County Attributes—Total U.S., 1969–2005 Counties. National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008, based on the November 2007 submission. Accessed December 2009.
10. Devesa SS, Donaldson J, Fears T: Graphical presentation of trends in rates. *Am J Epidemiol* 1995; 141: 300–4.
11. Tiwari RC, Clegg LX, Zou Z: Efficient interval estimation for age-adjusted cancer rates. *Stat Methods Med Res* 2006; 15: 547–69.
12. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Databases: Incidence—SEER 17 Regs Limited Use + Hurricane Katrina Impacted Louisiana Cases, November 2008 Sub (1973–2006 varying)—Linked To County Attributes—Total U.S., 1969–2006 Counties. National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2009, based on the November 2008 submission. Accessed December 2009.
13. McGlynn KA, Devesa SS, Graubard BI, Castle PE: Increasing incidence of testicular germ cell tumors among black men in the United States. *J Clin Oncol* 2005; 23: 5757–61.
14. McGlynn KA, Devesa SS, Sigurdson AJ, Brown LM, Tsao L, Tarone RE: Trends in the incidence of testicular germ cell tumors in the United States. *Cancer* 2003; 97: 63–70.

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