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Distribution of Serum Tumor Markers for Testicular Cancer across Racial/Ethnic Groups from 2004 to 2007 in the United States

By

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Master of Public Health

Epidemiology

_____

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By

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B.A., University of Chicago, 2009

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An abstract of
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2011

ABSTRACT

Distribution of Serum Tumor Markers for Testicular Cancer across Racial/Ethnic Groups from 2004 to 2007 in the United States
By Tiffany Hosten

Objective: While the incidence of testicular cancer is lower among Non-Hispanic Black men compared to U.S. men of other races and ethnicities, Black testicular cancer patients have poorer survival. Social factors may account for this observed disparity in outcome, however, biological tumor characteristics including levels of prognostic testicular tumor markers such as alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH) have not previously been compared across racial and ethnic groups on a population level.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER) public-access dataset from 2004 through 2007, the distributions of tumor markers for testicular cancer cases were compared in three groups of patients: Non-Hispanic Whites, Non-Hispanic Blacks, and Hispanics. Association between elevated levels of each marker and race/ethnicity was examined using multivariate logistic regression models with results expressed as adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Results: We found that Hispanics were more likely than Non-Hispanic Whites to have elevated LDH with OR (95% CI) 1.5 (1.2-1.8), while the corresponding result for Blacks in comparison to Whites was 1.5 (1.0-2.5). No difference in frequency of elevated serum tumor marker levels was observed across race/ethnicity for AFP and hCG.

Conclusion: Racial/ethnic disparities in testicular cancer survival are more likely to be explained by the differences in early detection, access to care, care utilization, and quality of care than by the differences in biological tumor characteristics. Future studies should explore tumor marker distributions among additional racial groups and use SEER's new, more uniformly coded site-specific variables.

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BACKGROUND AND LITERATURE REVIEW

In the United States, testicular cancer accounts for 1% of all cancers in men and for 5% of male genitourinary malignancies (1, 2). Testes, the pair of male sex glands located behind the penis within a pouch of skin called the scrotum, are the main source of testosterone and the site of sperm production and storage (2). Testicular carcinomas are the most common solid tumor among men 15 to 34 years of age (2). According to estimates from the American Cancer Society, among U.S. men in 2010 there were 8,480 new cases of testicular cancer and 350 deaths from the disease (3). While the incidence of testicular cancer is lower among African-American men compared to U.S. men of other races and ethnicities, African-American testicular cancer patients have poorer survival (4-9). Delayed presentation, differences in adherence to follow-up, socioeconomic status, access to healthcare, education, culture, and lifestyle have been proposed as explanations that may account for this observed disparity in outcomes (3, 4, 8-11). However, biological tumor characteristics such as levels of prognostic tumor markers have not previously been compared across racial and ethnic groups on a population level.

Testicular cancer can occur in one or both testicles (2). This form of cancer is commonly detected via self-examination or during physical examination by a physician. Risk factors for testicular cancer include cryptorchidism, in which one or both testicles do not descend from the abdomen into the scrotum, and Klinefelter's syndrome, a genetic disorder in which males have at least one additional X-chromosome (2, 12). Other risk factors include family history, infertility, testicular atrophy, hypogonadism, testicular dysgenesis syndromes, and inguinal hernias (2, 12, 13). Ninety-five percent of testicular

cancers arise in germ cells, the cells that give rise to sperm, while the other 5% are non-germinal tumors (2). Carcinoma in situ, intratubular germ cell neoplasia (ITGCN), precedes the majority of invasive germ cell tumors in adults (12). Progression from ITGCN to invasive cancer occurs after a median of approximately 5 years (12). The two major types of germ cell carcinomas are seminomas and nonseminomas (2). Seminomas are slow-growing cells that are sensitive to radiation and chemotherapy (2, 13). These carcinomas account for 50% of germ cell tumors and are most common during the 4th decade of life (12). Nonseminomas can be purely one cell type or mixed tumors comprised of two or more of the following cell types: embryonal carcinoma, choriocarcinoma, yolk sac tumor, or teratoma (12). These tumors grow quickly, do not respond to radiation treatment, and often present during the 3rd decade of life (2, 12).

The United States has witnessed a more than 2-fold increase in testicular cancer incidence since the 1940's (10). The Surveillance, Epidemiology, and End Results (SEER) program, which now includes approximately 28% of the U.S. population, offers a valuable source of data suitable for studying testicular carcinomas (1). Analyzing SEER data from 1985 through 2000, McGlynn and Devesa reported incidence rates for testicular cancer of 6.0 per 100,000 people among Whites and 1.1 per 100,000 among African-Americans (5). Gleason examined SEER data from 1974 to 1999 and found that Hispanics and Blacks were diagnosed at a younger age than Whites, but that this earlier presentation was associated with more advanced disease (11).

Biggs and Schwartz also analyzed SEER data (1973-1999) and similarly observed that a greater proportion of African-Americans presented with distant disease in comparison to Non-Hispanic Whites (10). These authors reported that African-

Americans had a hazard of death from testicular cancer 2.2 times greater than Non-Hispanic Whites (10). After adjusting for histology, period of diagnosis, and tumor stage, the testicular cancer survival was significantly higher in Non-Hispanic Whites compared to African-Americans and Hispanic Whites (10). The cumulative mortality over the 27-year study period was approximately 12.5% and 7.5% among Blacks and Hispanic Whites, respectively (10).

Bridges et al. conducted an analysis of 215 testicular cancer patients from four Chicago teaching hospitals between 1977 and 1991 (8). While these authors did not find a statistically significant difference in stage or histological tumor type between Whites and Blacks, there was a statistically significant difference in 5-year disease-specific survival (Whites:88%, Blacks:71%) (8).

Recently, the American Joint Committee on Cancer and the International Union Against Cancer expanded their TNM staging classification of testicular tumors by adding tumor markers (14). The TNM classification previously accounted only for size of the primary tumor (T), regional lymph node involvement (N), and distant metastases (M). Tumor markers (S) were added due to their prognostic significance. These factors are clinically relevant as they are helpful in diagnosing cancer when measured prior to radical orchiectomy, a procedure through which a testicle is surgically removed, in treatment planning, and during management when measured post-treatment (2). The specific markers relevant to testicular cancer diagnosis and management include alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH) (2, 12, 14).

AFP: Alpha-fetoprotein is a single chain glycoprotein typically produced by the fetus (2, 14). As a major serum binding protein in the fetus, when present in an adult, AFP may indicate germ cell tumors (2, 14). AFP is secreted by embryonal cell carcinomas and approximately 90% of yolk sac tumors (12, 14). AFP is not produced by pure seminomas or choriocarcinomas (12, 14). Normal levels of AFP in adults are less than 15 ng/mL (12). This marker may be elevated in 10-20% of stage I, 20-40% of stage II, and 40-60% of advanced testicular cancers (12). While liver cancers and non-malignant diseases can also secrete AFP, it is possible to distinguish between the protein arising from testicular cancers and that produced by other sites (14).

hCG: Human chorionic gonadotropin is a hormone that circulates during pregnancy and may serve as a marker of primary cancers of the testis, liver, pancreas, and ovaries (2, 14). This glycoprotein is secreted by all choriocarcinomas, 40-60% of embryonal cell carcinomas, and 10-20% of pure seminomas (12, 14). Levels of serum hCG between 0-10 IU/L are considered normal (2, 15). In addition to their prognostic values, both AFP and hCG are widely used for monitoring response to treatment (14).

LDH: Lactate dehydrogenase, a cytoplasmic enzyme, is present in all living cells and is involved in energy production (2, 14). When detected in serum, LDH may indicate tissue damage and cancer (2, 14). In a healthy adult, LDH ranges from 48-115 IU/L (2). Sixty percent of advanced nonseminoma tumor cases and 80% of advanced seminoma cases present with elevated LDH (12).

The Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) offers a valuable source of data suitable for studies of

rare tumors such as testicular carcinomas. This large population-based program includes data from 17 registries that cover approximately 28% of the United States population, and collects data on cancer incidence and survival in the U.S (1). In addition, the registry compiles data on patient demographics, cancer stage, grade, and treatments, and vital statistics. SEER conducts a continual control and quality improvements program to ensure the collection of high quality data and has 98% case completeness (1, 16). Collection of tumor marker data began in 1998, but reporting of these variables as part of site-specific collaborative stage factors was not required until 2004 (16, 17).

The relatively poor testicular cancer outcomes among African-Americans underscore the importance of better understanding the nature of this disease. Although social factors such as access to care and care utilization may explain racial disparities in testicular cancer prognosis, it is also important to explore the differences in the biological features of testicular carcinomas across racial and ethnic groups. Through this population-based analysis, we aim to determine whether frequencies of the elevated levels of AFP, hCG, and/or LDH differ by race and ethnicity, and if so, whether these differences may explain, at least in part, the racial/ethnic disparities in testicular cancer prognosis.

METHODS

Data Source

Information on testicular cancer cases was retrieved from the National Cancer Institute's SEER database which collects demographic and clinical data on individuals with cancer. This analysis used data from 17 SEER registries, which include regional centers in San Francisco-Oakland, Connecticut, Metropolitan Detroit, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Metropolitan Atlanta, San Jose-Monterey, Los Angeles, Rural Georgia, California (excluding San Francisco, Los Angeles, and San Jose), Kentucky, Louisiana, New Jersey, and Alaska (18). The SEER program, which now includes approximately 28% of the U.S. population, offers a valuable source of data suitable for studying testicular carcinomas. While urban residents and foreign-born individuals may be overrepresented in this database in comparison to the general population of the United States, SEER is considered a valid and representative sample of U.S. residents (1).

Study Subjects

This study was submitted to the Institutional Review Board (IRB) of Emory University and did not require IRB review. This investigation did not meet the definition of "human subjects" research or the definition of a "clinical investigation" since SEER is a publically-available, de-identified dataset.

Data on testicular cancer cases were extracted from the SEER database using SEER*Stat (version 6.6.2) in a Case Listing Session. Under the Selection tab, in the area titled "Select Only," the boxes for "Malignant Behavior" and "Known Age" were checked, and initial selection criteria included the following:

a. {Site and Morphology.Primary Site - labeled} = 'C62.0-Undescended testis','C62.1-Descended testis','C62.9-Testis, NOS' AND
b. {Race, Sex, Year Dx, Registry, County.Year of diagnosis} = '2004','2005','2006','2007'

This data were exported into SAS software, version 9.2 (SAS Institute Inc, Cary, NC) and the following criteria were used to identify eligible cases of testicular cancer:

a. *Case selection*: SEER variable "Site Rec with Kaposi and mesothelioma" was coded "testis," International Classification of Diseases for Oncology, Third Edition SEER variable, "ICD-O-3 Hist/behave," had defined ICD-O-3 codes for testicular cancer, and individuals whose race/ethnicity was classified Non-Hispanic White, Non-Hispanic Black, or Hispanic.
b. *Case exclusion*: Second or more primary tumors listed for cases with multiple listings in dataset, unknown or unstaged SEER "Summary stage 2000 (1998+)," and unspecified SEER "ICD-O-3 Hist/behav" (i.e. malignant neoplasm, carcinoma, adenocarcinoma).

Analysis

Variables

SEER variables "Race recode (W, B, AI, API)" and "Origin recode NHIA (Hispanic, Non-Hisp)" were combined to produce a race/ethnicity variable that included the following racial/ethnic categories: Non-Hispanic White (White), Non-Hispanic Black (Black), and Hispanic. The latter category included individuals of Hispanic ethnicity regardless of race.

SEER variables “CS site-specific factor 1 (2004+)” (AFP), “CS site-specific factor 2 (2004+)” (hCG), and “CS site-specific factor 3 (2004+)” (LDH) were the primary outcome variables of interest. SEER variable CS site-specific factor 1 was considered within normal limits if coded 20 (<15 ng/mL), and was defined as elevated if coded 40 (15 – 1,000 ng/mL), 50 (1,001 - 10,000 ng/mL), or 60 (>10,000 ng /mL) (19). CS site-specific factor 2 was considered normal if coded 20 (<10 mIU/mL) (19). This variable was elevated if coded 40 (11 – 5,000 mIU/mL), 50 (5,000 - 50,000 mIU/mL), or 60 (>50,000 mIU/mL) (19). SEER variable CS site-specific factor 3 was considered normal if coded 20 (<115 IU/L), and elevated if coded 40 (116 – 173 IU/L), 50 (173 – 1,150 IU/L), or 60 (>1,150 IU/L) (19). All variables were considered missing if coded 0 (test not done), 80 (ordered, but results not in chart), or 999 (unknown or no information) (19).

Another site specific variable, CS site-specific factor 4 which provided information concerning radical orchiectomy (RO) was defined as ‘RO not performed’ if coded 0, “RO performed” if coded 1, and missing if coded 999 (unknown if radical orchiectomy performed) (19). CS site-specific factor 5 which characterized the size of tumor metastasis in the lymph nodes was considered missing if coded 998 (Regional lymph nodes involved, size of lymph node mass not stated) or 999 (Unknown if regional nodes involved, not documented in patient record) (19).

ICD-O-3 histology and behavior codes were combined into the following testicular cancer histologic categories: seminoma (9061, 9062, 9063, 9064/3), embryonal carcinoma (9070), yolk sac tumor (9071), teratoma (9080, 9082, 9084), mixed germ cell tumor (9081, 9085, 9101, 9102) , choriocarcinoma (9100), unspecified nonseminoma

(9065), unspecified testicular cancer (8000, 8010, 8012, 8140), non-germ cell (8631, 8640, 8650, 8800, 8801, 8900, 8910, 8912). The 17 SEER cancer registries were grouped into the U.S. Census Bureau's 4 geographical regions: Midwest (Metropolitan Detroit, Iowa), Northeast (Connecticut, New Jersey), South (Metropolitan Atlanta, Rural Georgia Kentucky, Louisiana), and West (San Francisco-Oakland, New Mexico, Seattle (Puget Sound), Utah, San Jose-Monterey, Los Angeles, California (excluding San Francisco, Los Angeles, and San Jose), and Alaska) (20).

Other variables of interest included age (SEER variable: Age at diagnosis), SEER Summary Stage (Summary stage 2000 (1998+); Localized, Regional, Distant), and the laterality of the testicular malignancy (Laterality (1973+)).

Statistical Analysis

Frequencies for descriptive statistics were generated and χ^2 tests were performed to compare the distributions of categorical variables between racial and ethnic groups. Unadjusted odds ratios accompanied by 95% confidence intervals (95% CI) were computed using logistic regression models that included only one variable of interest as a predictor. Adjusted odds ratios were obtained by including all variables of interest in a logistic regression model. Collinearity and interaction were assessed.

RESULTS

The total study population included 7,824 testicular cancer patients; of those 77.2% were White (N=6,042), 2.4% Black (N=191), and 20.3% Hispanic (N=1,591). There was a statistically significant difference between the proportions of racial and ethnic groups with regard to age at diagnosis, tumor histology and stage, laterality, region of residence, and county attributes (Table 1). The greatest proportion of Non-Hispanic Whites and Blacks were diagnosed between 30 to 39 years of age, while Hispanics were most frequently diagnosed between ages of 20 and 29. Seminomas were the most common histologic type among Blacks and Whites, whereas nonseminomas constituted more than one half of all testicular cancers among Hispanics. Blacks had an almost 10-fold greater proportion of non-germ cell tumors in comparison to Whites (6.81% versus 0.70%) and a 5-fold greater proportion in comparison to Hispanics (6.81% versus 1.32%). While only 10% of Whites were diagnosed with distant stage testicular cancer, 22% of Blacks and 18% of Hispanics had distant disease.

With respect to site-specific variables summarized in Table 2, a greater proportion of Hispanics (32%) had elevated levels of AFP and hCG in comparison to both Blacks (25%) and Whites (22%). Both Blacks and Hispanics had a larger proportion of testicular cancer cases with elevated LDH in comparison to Whites (24.61% and 22.75% versus 16.34%, respectively). Radical orchiectomy was not performed in 8% of cases in Blacks compared to 6% among Hispanics and 4% among Whites.

Characteristics of cases included in the analyses of elevated tumor markers (i.e. excluding those with missing values) in comparison to the entire dataset are displayed in Figure 1. The distributions of race/ethnicity, age, and histology were similar in the

overall group and across the subgroups of cases with known values for AFP, hCG, and LDH. However, a somewhat greater proportion of cases with regional and distant stage testicular cancer were present among patients with complete information on LDH relative to the other groups (Figure 1).

Tables 3 and 4 show the results of crude and adjusted associations of various patient- and disease-related characteristics to elevated levels of AFP, hCG, and LDH. There were no statistically significant associations between race/ethnicity and elevated AFP or hCG; however, Hispanics were more likely than Whites to have abnormal LDH with OR (95% CI) of 1.6 (1.4-1.9) in the crude analyses and 1.5 (1.2-1.8) after adjusting for age at diagnosis, tumor histology and stage, laterality, year of diagnosis, region of registry, and county attributes. While the unadjusted model indicated a statistically significant difference between Blacks and Whites with respect to elevated LDH, this difference was somewhat attenuated and was only borderline significant (OR=1.5; 95% CI: 1.0-2.5) after adjustment for confounders. Testicular cancer patients 19 years of age or younger were more likely to have elevated AFP compared to 30 – 39 year olds with an adjusted OR of 1.5 (95% CI: 1.1-2.0). Relative to the reference category of 30-39 years of age, cases between ages 20 and 29 years were less likely to have elevated LDH and individuals 50 years of age and older were less likely to have elevated hCG . Nonseminomas and distant stage cancers were associated with statistically significant elevated levels of tumor markers in both unadjusted and adjusted models. In the analyses by region, cases obtained from Southern SEER registries included a greater proportion of cases with elevated hCG levels (OR=1.4; 95% CI: 1.1-1.7) in comparison to Western registries.

DISCUSSION

In this analysis of SEER data covering a period between 2004 and 2007, the tumor makers of testicular cancer across racial and ethnic groups were similar. We observed no statistically significant associations between race/ethnicity and elevated levels of AFP or hCG, the tumor markers most specific to testicular malignancies. However, adjusted models revealed that Hispanics were more likely than Whites to have abnormal LDH while frequency of elevated LDH among Blacks in comparison to Whites approached, but did not reach, statistical significance. In addition, a greater proportion of Blacks presented with non-germinal tumors in comparison to both Whites and Hispanics. Biggs and Schwartz's investigation of 12 SEER registries between 1973 and 1999 yielded similar distributions in non-germ histology across race/ethnicity categories (10). Available literature on non-germinal cancers of the testis is sparse and is primarily comprised of case-reports. As non-germinal cancers are so rare, the Black-White differences in the frequency of this histologic tumor type are unlikely to explain the racial survival disparities among testicular cancer patients. Not directly related to the research questions of interest, but also worthy of note, radical orchiectomy was less common among Blacks in comparison to Hispanics and Whites although this therapeutic procedure is standard therapy for all testicular carcinomas (12, 21).

The main strength of this investigation is the use of a large population-based dataset. To our knowledge this is the first study to examine racial and ethnic distributions of tumor markers for testicular cancer. Additionally, we employed multivariate models to identify characteristics of testicular cancer cases that may be associated with elevated serum tumor markers after controlling for likely confounders. Limitations of our study

include the inconsistency of the variable used to analyze each tumor marker, the SEER collaborative stage (CS) site-specific variables. While these variables are retained in the SEER database, they are considered obsolete due to the ambiguous coding of tumor markers which do not distinguish between pre-orchiectomy versus post-orchiectomy values (19). Secondly, due to the complexity of AJCC tumor staging, a crude classification of stage that may not adequately capture the extent of disease was included in this investigation. Finally, the recent inclusion of tumor markers in the SEER registry limited this analysis to a 4-year period for assessing the elevation of serum tumor markers across racial and ethnic groups, resulting in relatively few cases among Blacks.

Future investigations should consider analyzing additional racial groups such as Native Americans and Asians. To underscore the importance of characterizing this disease in the American Indian community, Weir et al. studied cancer in individuals 20 to 44 years of age and discovered that 18% of cancers among males were from the genital system with testicular germ cell carcinomas accounting for approximately 90% of these genital cancers (22). With respect to Asians, Biggs and Schwartz found that Chinese, Japanese, and Filipinos were more likely than other racial and ethnic groups to be diagnosed with localized disease (10). In addition, assessing SEER site-specific factors 6 through 10 in future analyses, variables that code for pre-orchiectomy levels of serum tumor markers, may provide better understanding of the racial/ethnic differences in biological properties of testicular tumors. CS site-specific factor 11 which indicates whether tumor markers remained elevated after radical orchiectomy can be used in conjunction with the pre-orchiectomy values to analyze differences in response to treatment across racial and ethnic groups (19). Also, when additional years of data

become available, linking levels of tumor markers to survival may help assess their prognostic value on a population level.

In summary, we did not find any statistically significant difference in the frequency of elevated tumor markers most specific to testicular cancer – AFP and hCG. On the other hand, our data suggest that levels of LDH and the frequency of non-germinal tumors may indeed be different in Non-Hispanic Whites than in other racial/ethnic groups, although the prognostic implications of these findings, if any, are not clear. We conclude that the well-documented racial/ethnic disparities in testicular cancer survival are more likely to be explained by the differences in early detection, access to care, care utilization, and quality of care than by the differences in biological tumor characteristics.

REFERENCES

1. Surveillance, Epidemiology, and End Results (http://seer.cancer.gov/). (Accessed January 30, 2011).
2. National Cancer Institute. (http://www.cancer.gov/). (Accessed January 28, 2011).
3. Society AC. Cancer Facts & Figures 2010. 2010.
4. Gajendran VK, Nguyen M, Ellison LM. Testicular cancer patterns in African-American men. *Urology* 2005;66(3):602-5.
5. McGlynn KA, Devesa SS. Re: Nguyen MM, Ellison LM: Testicular cancer patterns in Asian-American males: an opportunity for public health education to impact outcomes (Urology 66: 606-609, 2005) and Gajendran VK, Nguyen M, Ellison LM: Testicular cancer patterns in African-American men (Urology 66: 602-605, 2005). *Urology* 2008;71(2):356-7.
6. McGlynn KA, Devesa SS, Graubard BI, et al. Increasing incidence of testicular germ cell tumors among black men in the United States. *J Clin Oncol* 2005;23(24):5757-61.
7. Shah MN, Devesa SS, Zhu K, et al. Trends in testicular germ cell tumours by ethnic group in the United States. *Int J Androl* 2007;30(4):206-13; discussion 13-4.
8. Bridges PJ, Sharifi R, Razzaq A, et al. Decreased survival of black Americans with testicular cancer. *J Urol* 1998;159(4):1221-3.
9. Holmes L, Jr., Escalante C, Garrison O, et al. Testicular cancer incidence trends in the USA (1975-2004): plateau or shifting racial paradigm? *Public Health* 2008;122(9):862-72.

10. Biggs ML, Schwartz SM. Differences in testis cancer survival by race and ethnicity: a population-based study, 1973-1999 (United States). *Cancer Causes Control* 2004;15(5):437-44.

11. Gleason AM. Racial disparities in testicular cancer: impact on health promotion. *J Transcult Nurs* 2006;17(1):58-64.

12. Bosl GJ, Bajorin DF, Sheinfeld J, et al. Cancer of the Testis In: Devita, Hellman, Rosenberg, eds. *Devita, Hellman, & Rosenberg's Cancer: Principles and Practice of Oncology*, 2008.

13. Hayes-Lattin B, Nichols CR. Testicular cancer: a prototypic tumor of young adults. *Semin Oncol* 2009;36(5):432-8.

14. Ehrlich Y, Beck SD, Foster RS, et al. Serum tumor markers in testicular cancer. *Urol Oncol* 2010.

15. Gilligan TD, Seidenfeld J, Basch EM, et al. American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. *J Clin Oncol* 2010;28(20):3388-404.

16. Goodman M, Ward K. Frequency and Predictors of Missing Data in Site-Specific Variables Recently Added to SEER. *N01-PC-95002-18 SEER Rapid Response Surveillance Study*. Atlanta: Emory University, Rollins School of Public Health, 2010.

17. Gilbert SM, Daignault S, Weizer AZ, et al. The use of tumor markers in testis cancer in the United States: a potential quality issue. *Urol Oncol* 2008;26(2):153-7.

18. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 17 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2009 Sub (1973-2007 varying) - Linked To County Attributes - Total U.S., 1969-2007 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2010, based on the November 2009 submission.

19. Collaborative Stage for TNM 7: Testis. SEER. (http://web2.facs.org/cstage202/testis/Testisschema.html). (Accessed February 20, 2011).

20. Census Regions and Divisions of the United States. U.S. Department of Commerce Economics and Statistics Administration U.S. Census Bureau: Geography Division.

21. Risk MC, Porter CR. Management of non-germinal testicular tumors. *World J Urol* 2009;27(4):507-12.

22. Weir HK, Jim MA, Marrett LD, et al. Cancer in American Indian and Alaska Native young adults (ages 20-44 years): US, 1999-2004. *Cancer* 2008;113(5 Suppl):1153-67.

TABLES

Table 1. Characteristics of testicular cancer cases by race and ethnicity: SEER -17, 2004-2007

	All cases (N=7,824)		Race/Ethnicity						
			White (N=6,042)		Black (N=191)		Hispanic (N=1,591)		
	No.	%	No.	%	No.	%	No.	%	
Age									
0-19 years	459	5.87	288	4.77	15	7.85	156	9.81	**
20-29 years	2,449	31.30	1667	27.59	49	25.65	733	46.07	
30-39 years	2,415	30.87	1896	31.38	59	30.89	460	28.91	
40-49 years	1,677	21.43	1439	23.82	50	26.18	188	11.82	
50+ years	824	10.53	752	12.45	18	9.42	54	3.39	
Histology									
Germ Cell									
Seminoma	4,391	56.12	3557	58.87	109	57.07	725	45.57	**
Nonseminoma†	3,357	42.91	2443	40.43	69	36.13	845	53.11	
Choriocarcinoma	52	1.64	28	1.21	2	3.13	22	2.78	
Embryonal Carcinoma	694	21.84	547	23.56	9	14.06	138	17.45	
Mixed Germ Cell Tumor	2,219	69.85	1607	69.21	47	73.44	565	71.43	
Teratoma	106	3.34	72	3.10	4	6.25	30	3.79	
Yolk Sac Tumor	106	3.34	68	2.93	2	3.13	36	4.55	
Non-Germ Cell	76	0.97	42	0.70	13	6.81	21	1.32	
Stage									
Localized	5,453	69.70	4347	71.95	118	61.78	988	62.10	**
Regional	1,416	18.10	1071	17.73	31	16.23	314	19.74	
Distant	955	12.21	624	10.33	42	21.99	289	18.16	
Laterality									
Origin of Primary- Right Only	4,081	52.16	3153	52.18	92	48.17	836	52.55	
Other	3,743	47.84	2889	47.82	99	51.83	755	47.45	
Year									
2004	2,010	25.69	1588	26.28	48	25.13	374	23.51	
2005	1,949	24.91	1530	25.32	48	25.13	371	23.32	
2006	1,916	24.49	1457	24.11	48	25.13	411	25.83	
2007	1,949	24.91	1467	24.28	47	24.61	435	27.34	
Region									
Midwest	755	9.65	707	11.70	27	14.14	21	1.32	**
North	1,270	16.23	1093	18.09	30	15.71	147	9.24	
South	976	12.47	871	14.42	64	33.51	41	2.58	
West	4,823	61.64	3371	55.79	70	36.65	1382	86.86	
County attributes									
Metro ≥1 mil. pop.	4,961	63.41	3692	61.11	142	74.35	1127	70.84	**
Metro between 250,000-1 mil. pop.	1,583	20.23	1232	20.39	27	14.14	324	20.36	
Other	1,280	16.36	1118	18.50	22	11.52	140	8.80	

[a] Percentages may not sum to 100% due to rounding.

†More cases are represented as nonseminoma than in nonseminoma histological sub-types since some tumors were categorized “Germ cell tumor, nonseminomatous” without further specification.

*p <0.05

**p<0.01

Table 2. Distribution of SEER's testicular cancer site specific variables by race and ethnicity

Site Specific Variables	All cases (N=7,824)		Race/Ethnicity						
			White (N=6,042)		Black (N=191)		Hispanic (N=1,591)		
	No.	%[a]	No.	%[a]	No.	%[a]	No.	%[a]	
AFP									
Normal	4,083	52.19	3258	53.92	96	50.26	729	45.82	**
Elevated	1,909	24.40	1352	22.38	47	24.61	510	32.06	
Missing	1,832	23.42	1432	23.70	48	25.13	352	22.12	
hCG									
Normal	3,598	45.99	2856	47.27	78	40.84	664	41.73	**
Elevated	2,224	28.43	1651	27.33	56	29.32	517	32.50	
Missing	2,002	25.59	1,535	25.41	57	29.84	410	25.77	
LDH									
Normal	2,185	27.93	1751	28.98	44	23.04	390	24.51	**
Elevated	1,396	17.84	987	16.34	47	24.61	362	22.75	
Missing	4,243	54.23	3,304	54.68	100	52.36	839	52.73	
Radical Orchiectomy									
Not performed	338	4.32	229	3.79	16	8.38	93	5.85	**
Performed	7,431	94.98	5767	95.45	175	91.62	1489	93.59	
Unknown	55	0.70	46	0.76	0	0.00	9	0.57	
Size of Lymph Node Metastasis									
None	5,650	72.21	4443	73.54	125	65.45	1082	68.01	**
≤2 cm, No extranodal extension	322	4.12	237	3.92	14	7.33	71	4.46	
2-5 cm, Extranodal extension	355	4.54	274	4.53	7	3.66	74	4.65	
>5 cm	312	3.99	222	3.67	11	5.76	79	4.97	
Missing	1,185	15.15	866	14.33	34	17.80	285	17.91	

[a] Percentages may not sum to 100% due to rounding.
*p <0.05
**p<0.01

Table 3. Unadjusted odds ratios for elevated testicular cancer tumor markers

Case Characteristics	AFP			hCG			LDH		
	OR	95% CI		OR	95% CI		OR	95% CI	
Race/Ethnicity									
White	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Black	1.2	0.8	1.7	1.2	0.9	1.8	1.9	1.2	2.9 *
Hispanic	1.7	1.5	1.9 *	1.3	1.2	1.5 *	1.6	1.4	1.9 *
Age									
30-39 years	1.0	(reference)		1.0	(reference)		1.0	(reference)	
0-19 years	5.0	4.0	6.4 *	2.7	2.1	3.4 *	1.6	1.2	2.2 *
20-29 years	2.0	1.7	2.3 *	1.6	1.4	1.8 *	1.1	0.9	1.3
40-49 years	0.7	0.6	0.8	0.8	0.7	1.0	1.0	0.8	1.2
50+ years	0.5	0.4	0.6	0.6	0.5	0.8	0.8	0.7	1.1
Histology									
Germ Cell									
Seminoma	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Nonseminoma	19.0	16.4	22.0 *	3.8	3.4	4.3 *	1.9	1.7	2.2 *
Non-Germ Cell	1.1	0.3	3.6	0.3	0.1	1.1	0.8	0.3	2.0
Stage									
Localized	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Regional	1.4	1.3	1.7 *	1.6	1.4	1.9 *	2.7	2.3	3.2 *
Distant	4.7	4.0	5.5 *	5.2	4.3	6.1 *	10.2	8.1	12.9 *
Laterality									
Origin of Primary- Right Only	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Other	1.1	1.0	1.2	1.0	0.9	1.1	1.0	0.9	1.1
Year									
2004	1.0	(reference)		1.0	(reference)		1.0	(reference)	
2005	1.1	0.9	1.2	0.9	0.8	1.1	1.0	0.8	1.2
2006	1.1	1.0	1.3	1.0	0.8	1.1	1.1	0.9	1.4
2007	1.1	0.9	1.2	1.0	0.9	1.2	1.1	0.9	1.3
Region									
West	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Midwest	0.9	0.7	1.0	1.0	0.8	1.2	1.0	0.8	1.2
North	0.7	0.6	0.9 *	0.7	0.6	0.8 *	0.7	0.6	0.8 *
South	1.0	0.8	1.2	1.2	1.0	1.4	1.1	0.9	1.4
County attributes									
Metro ≥1 mil. pop.	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Metro between 250,000-1 mil. pop.	0.9	0.8	1.1	1.1	0.9	1.2	1.0	0.9	1.2
Other	1.1	1.0	1.3	1.2	1.0	1.4	0.9	0.7	1.1

*p <0.05

Table 4. Full "gold standard" model showing adjusted odds ratios for elevated testicular cancer tumor markers[a]

Case Characteristics	AFP			hCG			LDH		
	OR	95% CI		OR	95% CI		OR	95% CI	
Race/Ethnicity									
White	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Black	1.3	0.8	2.1	1.2	0.8	1.8	1.5	1.0	2.5
Hispanic	1.2	1.0	1.5	1.1	0.9	1.2	1.5	1.2	1.8 *
Age									
30-39 years	1.0	(reference)		1.0	(reference)		1.0	(reference)	
0-19 years	1.5	1.1	2.0 *	1.3	1.0	1.7	0.9	0.7	1.3
20-29 years	1.0	0.9	1.2	1.1	0.9	1.3	0.8	0.6	0.9 *
40-49 years	0.9	0.7	1.1	0.8	0.7	1.0	1.0	0.8	1.2
50+ years	0.8	0.6	1.0	0.8	0.6	0.9 *	0.9	0.7	1.2
Histology									
Germ Cell									
Seminoma	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Nonseminoma	15.7	13.4	18.4 *	2.9	2.6	3.3 *	1.3	1.1	1.6 *
Non-Germ Cell	0.8	0.2	2.8	0.2	0.1	0.7 *	0.4	0.1	1.1
Stage									
Localized	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Regional	0.9	0.8	1.1	1.4	1.2	1.6 *	2.7	2.2	3.2 *
Distant	2.4	1.9	2.9 *	3.7	3.1	4.4 *	9.3	7.3	11.8 *
Laterality									
Origin of Primary- Right Only	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Other	1.1	0.9	1.2	0.9	0.8	1.0	1.0	0.8	1.1
Year									
2004	1.0	(reference)		1.0	(reference)		1.0	(reference)	
2005	1.0	0.8	1.2	0.9	0.7	1.0	1.0	0.8	1.2
2006	1.1	0.9	1.3	0.9	0.8	1.1	1.1	0.9	1.4
2007	0.9	0.8	1.1	0.9	0.8	1.1	1.1	0.9	1.3
Region									
West	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Midwest	0.9	0.7	1.2	1.0	0.8	1.3	1.2	1.0	1.6
North	0.9	0.8	1.1	0.8	0.7	1.0	0.8	0.6	1.0
South	1.3	1.0	1.6	1.4	1.1	1.7 *	1.3	1.0	1.7
County attributes									
Metro ≥1 mil. pop.	1.0	(reference)		1.0	(reference)		1.0	(reference)	
Metro between 250,000-1 mil. pop.	0.9	0.8	1.1	1.1	0.9	1.2	1.0	0.8	1.2
Other	1.1	0.9	1.4	1.1	1.0	1.3	0.9	0.7	1.1

[a]Model includes all variables listed in table.
*p <0.05

FIGURES AND FIGURE LEGENDS

Figure 1. Characteristics of sample populations used in analysis of each tumor marker.