Chapter 21
Cancer of the Testis

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INTRODUCTION

Testicular cancer is a relatively rare cancer, with an estimated 8,250 new cases diagnosed in U.S. men in 2006 (1). Despite the fact that it accounts for only 1% of all malignancies in males, it is the most common malignancy in men aged 20-34, and in the U.S. and most western countries the incidence has more than doubled since the 1940s (2,3). Survival of patients with testicular, particularly those with metastatic disease, has improved significantly since the early 1970's as the result of the development and wide-spread use of cisplatin-containing combination chemotherapy. The 5-year survival rate for testicular cancer patients, including all stages, was 72% in 1970-1973, and 91% for patients diagnosed in 1983-1985 (4). For men diagnosed with testicular cancer during 1992-1998, the 5-yr survival rate was 95% (4), and today, testicular cancer is considered one of the most curable solid neoplasms (5).

MATERIALS AND METHODS

There were 12,978 adult cases of testicular cancer (other than testicular lymphomas) diagnosed from 1988 through 2001 and reported to the SEER program. A detailed description of the source of these data is given in the introductory chapter of this monograph. Table 21.1 shows the numbers of cases excluded from the present analysis, by reason. This chapter describes survival analysis of the remaining 11,606 histologically confirmed, first primary cases of adult testicular cancer diagnosed from 1988 through 2001 and reported to the SEER Program.

Histologic Classification

Germ cell carcinomas comprise the overwhelming majority (98.9%) of adult testicular carcinomas (6). Because non-germ cell testis tumors are uncommon and comprise a heterogeneous group, the focus of the analysis was on germ cell carcinomas. Within the germ cell neoplasms, tumors can be classified, based on pathologic and clinical features, into two broad histologic groups: seminomas and non-seminomas. Seminomas tend to grow more slowly and are very sensitive to radiation therapy, compared to non-seminomas which are more clinically aggressive and do not respond well to radiotherapy (7). Approximately 61% of testicular germ cell carcinomas are pure seminomas with the remainder comprised of non-seminomas (teratomas, embryonal carcinomas, choriocarcinomas, yolk sac tumors), and mixtures of two or more types (8). Germ cell carcinomas were classified using ICD-O-2/ICD-O-3 morphology codes into broad categories of seminoma (ICD 9060-9064) and non-seminoma (ICD 9070-9101), or more narrowly into specific histologic groups: seminoma (ICD 9060-9064), embryonal carcinoma (ICD 9070), yolk sac tumor (ICD 9071), teratoma (ICD 9080, 9082-9084), mixed

Table 21.1: Cancer of the Testis: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
12,978	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
12,528	450	Select first primary only
12,511	17	Exclude death certificate only or at autopsy
12,394	117	Exclude unknown race
12,366	28	Exclude alive with no survival time
11,707	659	Exclude children (Ages 0-19)
11,699	8	Exclude in situ cancers
11,651	48	Exclude no or unknown microscopic confirmation
11,606	45	Exclude sarcomas

germ cell tumor (ICD 9081, 9085, 9101), and choriocarcinoma (ICD 9100).

Stage

Testicular cancers are staged within the SEER data using the categories in situ, localized, regional, distant, and unstaged. Staging information on the cancer is also contained within the 10-digit Extent of Disease (EOD) code, which is based on clinical, operative, and pathologic diagnoses of the cancer. The EOD code encodes tumor size, extension of the tumor into surrounding tissues, and lymph node involvement. We used EOD coding to stage tumors according to the American Joint Committee on Cancer (AJCC) classification system, 5th Edition (9). The SEER modified AJCC stages (5th edition) for testicular cancer are as follows: Stage I (no spread to lymph nodes or distant organs), Stage II (the cancer has spread to regional lymph nodes but not to lymph nodes in other parts of the body or to distant organs), and Stage III (the cancer has spread to non regional lymph nodes and/or to distant organs). We were not able to further subclassify stages (ie., A, B, C) because substaging relies on serum tumor marker data which was not collected by the SEER program prior to 1998.

Tumor Size

Information on tumor size is contained within the 10-digit Extent of Disease (EOD) code. We examined the influence of tumor size (< 5 cm vs. 5+ cm) on relative survival among patients diagnosed with Stage I testicular cancer.

Age & Race

To investigate the impact of age at diagnosis on relative survival, testicular cancer cases were grouped into the following age groups: 20-29, 30-39, 40-49, 50-59, 60-69, 70+. To examine race-specific survival, patients were classified into 3 groups: black, white and all (includes blacks, whites, and all other races).

RESULTS

Table 21.2 shows the frequency of testicular cancer cases classified by histology and age at diagnosis. Seminomas comprised the largest histologic group (61.1%). Germ cell tumors of mixed histologic types comprised the next largest group (23.2%). Non-germ cell and unspecified tumors comprised 1% of eligible tumors. More than 72% of the testicular cancer cases were diagnosed between the ages of 20-39. For men diagnosed with seminomas, the peak frequency occurred in the 30-39 year age group, while for men diagnosed with non-seminomas it was among 20-29 year olds.

Three-quarters of all men with testicular carcinomas were diagnosed in Stage I (Table 21.3). However, the proportion of tumors diagnosed at early and late stages varied with the histologic type of the tumor. The largest proportion of testis tumors diagnosed in Stage I were seminomas (85.8%). Choriocarcinomas had the smallest proportion of Stage I tumors (20.7%) and the largest proportion of Stage III tumors (74.1%).

Overall Survival

Overall, survival among men diagnosed with testicular cancer was very high. Relative survival rate was 98% at 1 year following diagnosis, 97% at 2 years, 96% at 5 year, and 95% at 10 years after diagnosis (Table 21.4).

Histology

The relative survival rate varied with the histologic type of the tumor (Figure 21.1). The highest survival rate was observed for men diagnosed with pure seminomas; 10-year relative survival was 98. The 10-year relative survival

Table 21.2: Cancer of the Testis: Number and Distribution of Cases by Histology and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)							
	Total		20-29	30-39	40-49	50-59	60-69	70+
Histology	Cases	Percent	Cases	Cases	Cases	Cases	Cases	Cases
Total	11,606	100.0	3,663	4,746	2,329	581	196	91
Germ Cell	11,480	98.9	3,639	4,710	2,307	563	183	78
Seminomas	7,086	61.1	1,471	3,137	1,802	455	153	68
Non-seminomas	4,394	37.9	2,168	1,573	505	108	30	10
Embryonal	1,315	11.3	624	479	164	36	8	<5
Yolk Sac	126	1.1	56	46	17	<5	<5	<5
Teratoma	203	1.7	117	62	21	<5	0	<5
Mixed Germ Cell	2,692	23.2	1,344	968	294	65	17	<5
Choriocarcinoma	58	0.5	27	18	9	<5	<5	0
Non-Germ Cell and Unspecified	126	1.1	24	36	22	18	13	13

Table 21.3: Cancer of the Testis: Number and Distribution of Cases by Histology and AJCC Stage (SEER modified 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage									
	Total		I		II		III		Unknown/ Unstaged	
Histology	Cases	Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent
Total	11,606	100.0	8,847	76.2	1,343	11.6	1,214	10.5	202	1.7
Germ Cell	11,480	100.0	8,781	76.5	1,340	11.7	1,175	10.2	184	1.6
Seminomas	7,086	100.0	6,077	85.8	507	7.2	393	5.5	109	1.5
Non-seminomas	4,394	100.0	2,704	61.5	833	19.0	782	17.8	75	1.7
Embryonal	1,315	100.0	728	55.4	339	25.8	226	17.2	22	1.7
Yolk Sac	126	100.0	72	57.1	18	14.3	34	27.0	<5	1.6
Teratoma	203	100.0	145	71.4	27	13.3	24	11.8	7	3.4
Mixed Germ Cell	2,692	100.0	1,747	64.9	449	16.7	455	16.9	41	1.5
Choriocarcinoma	58	100.0	12	20.7	0	0.0	43	74.1	<5	5.2
Non-Germ Cell and Unspecified	126	100.0	66	52.4	<5	2.4	39	31.0	18	14.3

rate for non-seminomas was lower, 91% (Table 21.4), but varied by histologic type from 46% for choriocarcinoma to 92% for embryonal tumors and mixed germ cell tumors (Figure 21.1).

Stage and histology

Testicular cancer relative survival decreased with increasing stage at diagnosis. Ten-year relative survival rates were over 95% for both Stage I and Stage II. When comparing tumors diagnosed at the same stage, survival rates for seminomas and non-seminomas were similar, with the exception of tumors diagnosed at Stage III (Table 21.4). Among men diagnosed with advanced disease, those diagnosed with seminomas had substantially better 2-, 3-, 5-, 8-, and 10- year survival rates than men diagnosed with non-seminomas.

Tumor size

Relative survival of patients diagnosed with Stage I testicular cancer was higher for those with tumors smaller than 5 cm compared to patients diagnosed with tumors that were 5 cm or larger (Table 21.5). Size accounted for more of a survival difference for non-seminomas than seminomas, but 10-year survival rates were over 92% even for non-seminomas 5 cm and over.

Age at Diagnosis

Among men diagnosed with seminomas, those aged 20-49 had similar, though slightly higher, survival to those over 50 years (Fig. 21.2). Among men with non-seminomas, the difference in survival between the two age groups was more pronounced: 2-year survival rate was 95% in the younger age group versus 84% in the older one; 5-year survival rate was 93% in the 20-49 age group versus 79% in those over 50 years of age. The distribution of stage at diagnosis of testicular tumors was similar among men aged 20-49 and those aged 50+ (results not shown).

Race

For seminomas, survival was slightly less among black men than among white men (Fig. 21.3). The disparity was more marked among men diagnosed with non-seminomas; 5-year relative survival rate was 93% among white men diagnosed with non-seminomas compared to 75% among black men. The distribution of specific histologic types did not vary appreciably by race (results not shown).

Race and Stage

Black men were more likely to be diagnosed with higher stage germ cell carcinomas compared to white men (Table 21.6). For any given stage, the relative survival rate among black men was poorer than survival rate among white men (Table 21.7). The racial disparity was most pronounced among patients diagnosed in Stage III; 5-year relative survival rate among white men was 75% compared to 58% among black men. Black men had larger tumors, on average, than white men diagnosed at the same stage (results not shown).

DISCUSSION

Overall, the survival rates for patients diagnosed with testicular cancer during 1988-2001 was excellent, with 95% surviving 10 years. Improvements in treatment, the most dramatic resulting from the introduction of cisplatin-containing combination chemotherapy in the 1970's, have

Table 21.4: Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition) and Histology, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage/Histology	Cases	Relative Survival Rate (%)					
		1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	11,480	98.2	96.8	96.2	96.0	95.4	95.3
Seminomas	7,086	99.0	98.4	98.1	98.0	97.7	97.7
Non-seminomas	4,394	96.8	94.2	93.2	92.6	91.8	91.3
Stage I	8,781	99.8	99.4	99.0	99.0	98.6	98.5
Seminomas	6,077	100.0	99.7	99.5	99.5	99.4	99.4
Non-seminomas	2,704	99.5	98.5	97.8	97.5	96.8	96.5
Stage II	1,340	98.5	97.0	96.5	96.1	95.5	95.2
Seminomas	507	98.4	96.8	96.3	95.9	95.1	95.1
Non-seminomas	833	98.5	97.1	96.6	96.0	95.7	94.9
Stage III	1,175	85.8	78.1	75.3	74.0	71.5	71.1
Seminomas	393	85.9	81.9	79.3	78.5	75.2	74.7
Non-seminomas	782	85.7	76.2	73.3	71.7	69.7	68.7
Unknown/Unstaged	184	97.4	94.9	93.9	93.1	93.1	93.1
Seminomas	109	96.5	94.0	93.2	93.2	93.2	93.2
Non-seminomas	75	98.7	96.2	95.0	92.2	92.2	92.2

Table 21.5: Stage I Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Histology/Tumor Size	Cases	Relative Survival Rate (%)					
		1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Germ Cell	8,781	99.8	99.4	99.0	99.0	98.6	98.5
< 5 cm	5,166	100.0	99.8	99.8	99.8	99.8	99.8
5+ cm	2,321	99.6	98.8	97.9	97.6	96.8	96.4
Unknown	1,294	99.3	98.4	97.3	97.0	96.0	95.5
Seminomas	6,077	100.0	99.7	99.5	99.5	99.4	99.4
< 5 cm	3,497	100.0	100.0	100.0	100.0	100.0	100.0
5+ cm	1,671	99.8	99.3	98.6	98.4	97.9	97.8
Unknown	909	99.4	98.9	98.3	98.1	96.9	96.6
Non-seminomas	2,704	99.5	98.5	97.8	97.5	96.8	96.5
< 5 cm	1,669	99.7	99.2	99.1	99.1	98.9	98.9
5+ cm	650	99.1	97.6	96.0	95.3	93.0	92.4
Unknown	385	98.8	97.3	95.0	94.0	93.7	92.5

Figure 21.1: Cancer of the Testis: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

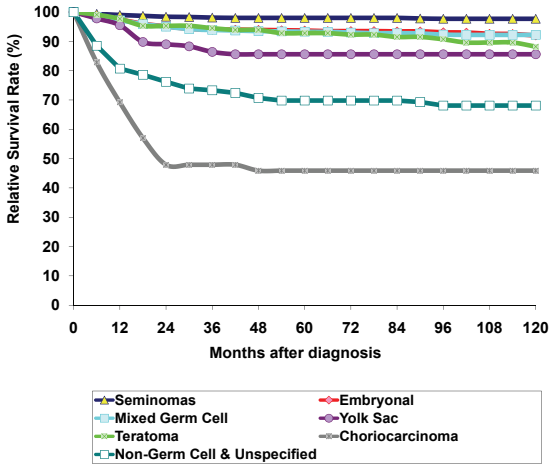


Figure 21.2: Cancer of the Testis: Relative Survival Rates (%) Histology and Age Group (20+), 12 SEER Areas, 1988-2001

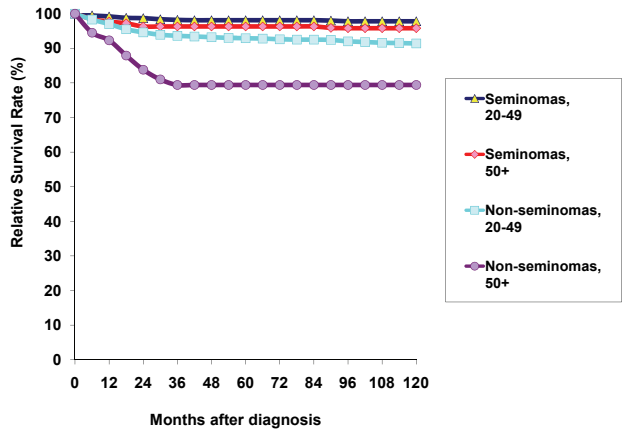


Table 21.6: Germ Cell Carcinoma of the Testis: Number and Distribution of Cases by AJCC Stage (SEER modified 5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Race					
	Total		White		Black	
	Cases	Percent	Cases	Percent	Cases	Percent
Total	11,480	100.0	10,711	100.0	250	100.0
Stage I	8,781	76.5	8,208	76.6	181	72.4
Stage II	1,340	11.7	1,253	11.7	30	12.0
Stage III	1,175	10.2	1,073	10.0	36	14.4
Unknown/ Unstaged	184	1.6	177	1.7	3	1.2

led to improved survival and declining mortality over the past 30 years (5).

Survival of patients with testicular cancer varied by the histologic type of the tumor, and differences in stage at diagnosis are likely to have contributed to this variation. Patients diagnosed with pure seminomas (predominantly diagnosed in Stage I) had the best survival; 10-year survival was 98%. Compared to those with seminomas, patients diagnosed with non-seminomas tended to be diagnosed with a more advanced stage of disease and had poorer survival, reflecting the more clinically aggressive nature of non-seminomas. Patients diagnosed with choriocarcinomas (largely diagnosed in Stage III) had the poorest survival.

Among non-seminoma testicular cancer patients diagnosed at Stage I, tumor size was related to survival. Patients diagnosed with tumors smaller than 5 cm experienced better relative survival than those diagnosed with tumors that were 5 cm or larger. For Stage I non-seminomas, the five-year survival among those with smaller tumors (< 5 cm) was 99% compared to 95% for patients diagnosed with larger tumors (5+ cm).

The age at diagnosis of testicular cancer had an impact on survival, particularly among men diagnosed with non-seminomas. Men diagnosed with non-seminomas between the ages of 20 and 49 had a 5-year survival of 93%, compared to 79% for those aged 50 and above. Stage at diagnosis was similar between younger and older men and could not account for the difference in survival observed.

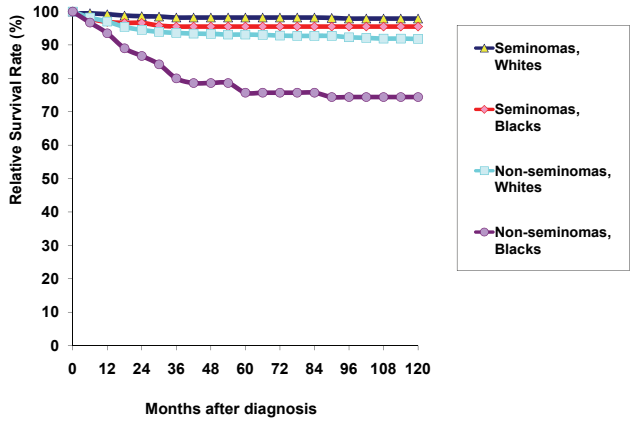
Testicular cancer survival also depended on the race of the patient, with black men experiencing poorer survival than white men. The differences in race-specific survival were partially explained by disease stage at diagnosis; compared to whites, a higher proportion of black men were diagnosed with advanced-stage disease. However, even when comparing men diagnosed at the same stage, survival was worse among black men compared to white men. The disparity in survival was particularly apparent among patients diagnosed with Stage III cancer; 5-year survival among men diagnosed with Stage III testicular cancer was 75% in white men compared to 58% in black men. The survival differential may be related to the larger average tumor size in black men, reflecting more advanced disease not captured in the 3-category staging classification that we used. Using these data, we were unable to explore the possible reasons for black men presenting with more advanced disease, nor whether this fully accounted for the survival differential between black and white testicular cancer patients.

Table 21.7: Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage/Race		Relative Survival Rate (%)					
	Cases	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Germ Cell	11,480	98.2	96.8	96.2	96.0	95.4	95.3
White	10,711	98.4	97.0	96.4	96.2	95.7	95.6
Black	250	95.8	93.5	90.2	89.7	89.7	89.7
Stage I	8,781	99.8	99.4	99.0	99.0	98.6	98.5
White	8,208	99.8	99.4	99.1	99.0	98.7	98.6
Black	181	99.3	99.1	95.6	95.6	95.6	95.6
Stage II	1,340	98.5	97.0	96.5	96.1	95.5	95.2
White	1,253	98.8	97.4	96.9	96.6	96.1	95.6
Black	30	97.1	93.8	90.3	86.1	86.1	86.1
Stage III	1,175	85.8	78.1	75.3	74.0	71.5	71.1
White	1,073	86.5	79.0	76.1	74.9	72.8	72.2
Black	36	75.5	63.7	60.6	57.5	54.2	54.2
Unknown/Unstaged	184	97.4	94.9	93.9	93.1	93.1	93.1
White	177	97.3	94.7	93.6	92.7	92.7	92.7
Black	3	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Figure 21.3: Cancer of the Testis: Relative Survival Rates (%) by Histology and Race, Ages 20+, 12 SEER Areas, 1988-2001



While survival of patients with testicular cancer is quite favorable in the 10 years following diagnosis, recent reports describe the occurrence of adverse health effects in long-term survivors more than 10 years after diagnosis. These include an increased risk of secondary malignant neoplasms (10) and cardiovascular events (11), some of which have been attributed to the radiation and chemotherapy treatments received by patients. Circulating levels of cisplatin may be detectable up to 20 years following treatment (12), for example. Given the early age of diagnosis and long life expectancy of most testicular cancer patients, consideration of these late effects is particularly important. Concern over long-term health effects, as well as more immediate quality-of-life issues (for instance, preservation of fertility) has led to the adoption of more conservative treatment regimens to minimize treatment-related morbidity. While in the past, patients with Stage I testis tumors routinely received additional treatment following orchiectomy, surgery followed by active surveillance alone is now a standard treatment option (13). Five-year survival rates for patients placed under active surveillance after orchiectomy as treatment for clinical Stage I seminomas appear to be comparable to those of patients treated with adjuvant radiation therapy (14-16). Similarly, 5-year survival does not appear to differ between patients undergoing retroperitoneal lymph node dissection (RPLND) and those entering a surveillance protocol after orchiectomy as treatment for clinical Stage I nonseminomatous testicular cancer (16,17).

In summary, testicular carcinoma remains one of the most highly curable malignant neoplasms. Additional research is needed to understand the reasons for the differences in the stage distribution of tumors according to race and the poorer survival of black patients and older patients, so that approaches to eliminating survival differences can be developed.

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