

Second Malignancies After Testicular Cancer

To the Editor: Testicular cancer has become the paradigm of a curable malignancy, with a 5-year relative survival rate of greater than 90%.¹ This markedly improved outlook underscores the need for quantitative data on the late complications of therapy, especially second malignancies. However, given the rarity of testicular cancer,¹ most surveys contain only small numbers of patients, as reviewed recently by Dieckmann et al,² precluding estimation of site-specific risks. To clarify these risks, we have quantified the occurrence of second malignancies among more than 9,700 men with testicular cancer, using resources of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (1973 to 1991) and the earlier years of the Connecticut Tumor Registry (1935 to 1972). These nine population-based cancer registries, which comprise approximately 10% of the United States population, also collect data on initial treatment for cancer in terms of broad categories. Surgery remains the cornerstone of treatment for testicular cancer, supplemented in some patients with regional radiotherapy.³ Chemotherapy has typically included various combinations of cisplatin, etoposide, vinblastine, and bleomycin.³ For our analyses, we grouped treatment into categories of surgery alone, radiotherapy, any chemotherapy, or other/no treatment.

Among 9,739 patients with testicular cancer who survived for at least 2 months, 315 second primary cancers developed (observed/expected [O/E] ratio, 1.56; 95% confidence interval [CI], 1.40 to 1.75) (Table 1). Significantly increased risks were observed for acute nonlymphocytic leukemia (ANLL), non-Hodgkin's lymphoma, and cancers of the rectum, prostate, kidney, bladder, and connective tissue. Significant excesses for all subsequent malignancies occurred in the 2 month to less than 1 year, 1 to 4+ year, 5 to 9+ year, and 10+ year intervals after testicular cancer (O/E ratios, 2.19, 1.36, 1.40, and 1.70, respectively). Ten-year survivors of seminoma had significantly increased risks for cancers of the pancreas (observed [Obs], 5; O/E, 3.23), kidney (Obs, 6; O/E, 3.22), bladder (Obs, 12; O/E, 2.94), and ANLL (Obs, 3; O/E, 5.77). Significant excesses of stomach (Obs, 4; O/E, 4.0) and connective tissue (Obs, 2; O/E, 10.80) neoplasms occurred among long-term survivors of nonseminoma. Among 2,786 10-year survivors of testicular cancer, significantly increased risks of solid tumors occurred among patients who initially received radiotherapy (Obs, 88; O/E, 1.76; 95% CI, 1.40 to 1.88), although excesses also followed treatment with surgery alone (Obs, 30; O/E, 1.40; 95% CI, 0.99 to 1.63), any chemotherapy (Obs, 6; O/E, 2.03; 95% CI, 0.89 to 2.32), or other/no treatment (Obs, 2; O/E, 1.40; 95% CI, 0.35 to 3.29). The largest risks for secondary ANLL occurred in men who received any chemotherapy (O/E, 21.4; 95% CI, 6.90 to 50).

Our results indicate the need to define better the role of treatment and other influences in the development of second neoplasms among patients with testicular cancer. Because little is known about the etiology of testicular neoplasia, which is increasing at a rate of 2% to 3% per year ($P < .05$),¹ the study of second malignancies assumes even greater importance for any insights that might be gained regarding shared etiologic influences, as well as therapy-related and diagnostic factors.

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Table 1. Risk of Second Malignancies After Testicular Cancer

	Seminoma*		Nonseminoma†		All Patients	
	Obs	O/E	Obs	O/E	Obs	O/E
No. of patients	5,065		4,674		9,739**	
No. person-years of follow-up	37,499		30,851		68,350	
Average age (years)‡	38.1		29.7		34.1	
All second cancers§	223	1.56	92	1.58	315¶	1.56
All solid tumors§	197	1.52	76	1.49	273	1.51
Mouth and pharynx	12	1.53	5	1.54	17	1.53
Esophagus	3	1.18	2	2.05	5	1.42
Stomach	5	1.07	5	2.47	10	1.50
Colon	16	1.21	7	1.36	23	1.25
Rectum	15	2.05	5	1.73	20	1.96
Pancreas	9	2.34	1	0.68	10	1.88
Lung	29	0.97	10	0.94	39	0.97
Prostate	40	1.91	16	2.22	56	1.99
Kidney	10	2.08	3	1.61	13	1.95
Bladder	24	2.46	5	1.34	29	2.15
Melanoma	10	1.71	4	1.29	14	1.56
Brain and CNS	5	1.61	1	0.59	6	1.25
Thyroid	3	2.27	2	2.47	5	2.34
Bone	0	—	0	—	0	—
Connective tissue	4	3.83	2	3.25	6	3.61
Non-Hodgkin's lymphoma	14	2.25	8	2.62	22	2.37
Hodgkin's disease	0	—	1	0.75	1	0.35
Multiple myeloma	2	1.21	0	—	2	0.88
ANLL	9	6.09	5	6.79	14	6.32
All others#	13	0.81	10	1.52	23	1.02

* ICD-0 morphology codes 9060-9064.

† All other first primary cancers of the testis that are not seminoma.

‡ Age at diagnosis of testicular cancer.

§ Numbers exclude second diagnoses of testicular cancer.

^{||} $P < .05$.

¶ 302 second cancers (96%) were microscopically confirmed.

Includes all cancers not specified above.

** Number represents 2-month survivors of testicular cancer. Patients were diagnosed between January 1, 1973 and December 31, 1991, and reported to one of nine population-based registries (including Connecticut), which participate in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program; patients in the earlier Connecticut cohort ($n = 917$) were diagnosed with testicular cancer between January 1, 1935 and December 31, 1972, and followed-up through December 31, 1988.

REFERENCES

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