GYNECOLOGY

Population-level trends in relative survival for cervical cancer

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OBJECTIVE: While the last 3 decades have seen numerous advances in the treatment of cervical cancer, it remains unclear if population-level survival has improved. We examined relative survival, the ratio of survival in cervical cancer patients to matched controls over time.

STUDY DESIGN: Patients with cervical cancer diagnosed from 1983 through 2009 and recorded in the Surveillance, Epidemiology, and End Results database were examined. Survival models were adjusted for age, race, stage, year of diagnosis, and time since diagnosis. Changes in stage-specific relative survival for patients with cervical cancer compared to the general population matched by age, race, and calendar year were examined over time.

RESULTS: A total of 46,932 patients were identified. For women with stage I tumors, the excess hazard ratio for women diagnosed in 2009 was 0.91 (95% confidence interval [CI], 0.86–0.95) compared to 2000, 0.81 (95% CI, 0.73–0.91) compared to 1990, and 0.75 (95% CI, 0.64–0.88) compared to 1983. For patients with stage III tumors, the excess hazard ratios for patients diagnosed in 2009 (relative to those diagnosed in 2000, 1990, and 1983) were 0.83 (95% CI, 0.80–0.87), 0.68 (95% CI, 0.62–0.75), and 0.59 (95% CI, 0.52–0.68). Similar trends in improved survival over time were noted for women with stage II tumors. There were no statistically significant improvements in relative survival over time for women with stage IV tumors.

CONCLUSION: Relative survival has improved over time for women with stage I-III cervical cancer, but has changed little for those with metastatic disease.

Key words: cervical cancer, cervical carcinoma, relative survival, survival, trends

Cite this article as: Wright JD, Chen L, Tergas AI, et al. Population-level trends in relative survival for cervical cancer. Am J Obstet Gynecol 2015;213:670.e1-7.

Cervical cancer remains a major cause of cancer-related mortality worldwide.[1] Over the last 3 decades, a number of treatment advances for cervical cancer have been demonstrated in clinical trials. For women with early-stage disease, newer surgical options are available and techniques for the delivery of radiation have improved. For advanced-stage disease, improved survival for the use of combination chemotherapy and radiotherapy resulted in a paradigm shift for patients with stage II-IV disease in 1999.[2-5] However, data describing how survival has changed over time remain limited.[6-11]

Quantifying changes in survival for cancer patients is of great importance as therapeutic advances that have shown efficacy in clinical trials are of little practical value if these treatments cannot be translated into clinical practice. However, examining secular trends in survival for cancer is methodologically challenging. First, as general medical care has improved over time, it is difficult to ascertain if improved survival for cancer patients is due to improved cancer treatment or due to greater longevity in the population as a whole.[12] Second, measuring cancer-specific survival is inherently difficult as data from death certificates are often inaccurate and may not reflect cancer-associated mortality in patients who die from complications and the sequelae of cancer.[13,14]

To quantify secular trends in survival for cancer patients, relative survival, the ratio of the observed survival rate for cancer patients to the expected survival rate of matched patients from the general population, has been described.[15-17] Relative survival is a useful metric that controls for changes in survival in the general population and describes excess mortality in cancer patients over time.[18,19] We performed a population-based analysis to examine secular changes in survival for women with cervical cancer treated in the United States from 1983 through 2009.

Materials and Methods

Data source

Data from the National Cancer Institute's Surveillance, Epidemiology, and

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Received April 3, 2015; revised June 7, 2015; accepted July 13, 2015.

J.D.W. (NCI R01 CA169121-01A1) and D.L.H. (NCI R01 CA166084) are recipients of grants and A.I.T. is the recipient of a fellowship (NCI R25 CA094061-11) from the National Cancer Institute.

The authors report no conflict of interest.

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0002-9378/$36.00 • http://dx.doi.org/10.1016/j.ajog.2015.07.012

End Results (SEER) database were used for analysis.[20] The SEER program comprehensively collects data on all newly diagnosed cancer patients from a number of registries located throughout the United States. We included patients with invasive cervical cancer diagnosed from January 1983 through December 2009 with follow-up through Dec. 31, 2011.

Data from the SEER 18 registries including San Francisco-Oakland, CA; Connecticut; Detroit, MI (metropolitan); Hawaii; Iowa; New Mexico; Utah; Seattle, WA (Puget Sound); Atlanta, GA (metropolitan); San Jose-Monterey, CA; Los Angeles, CA; Alaska Natives; rural Georgia; greater California; Kentucky; Louisiana; New Jersey; and greater Georgia were utilized. Louisiana cases diagnosed for July through December 2005 were excluded due to the impact of Hurricanes Katrina and Rita on the registry's ability to report data. Non-white and non-black women were excluded from the analyses since reliable population-level estimates of survival were required. Patients with unknown stage were excluded. The Columbia University Institutional Review Board deemed the study exempt.

Staging

Staging was based on the derived sixth edition of the American Joint Committee on Cancer (AJCC) staging for patients diagnosed from 2004 through 2009, and the SEER modified third edition of AJCC staging for those women diagnosed from 1988 through 2003.[20] Prior to 1988, AJCC staging was not recorded in SEER. For those women diagnosed prior to 1988, we constructed AJCC staging through the use of 4-digit extent of disease codes for patients treated in 1983 through 1987.[20]

Statistical analysis

The primary analysis focused on overall survival defined as the time from diagnosis of cervical cancer until death from any cause. Relative survival, the ratio of the observed survival rate for cancer patients to the expected survival rate of matched patients from the general population, was then estimated. Patients in the general population were matched to those with cervical cancer based on age, race, and calendar year using the Ederer II method calculated using SEER*Stat software.[21,22] Expected survival life tables were used to derive survival estimates for the controls. The expected life tables provide survival by age, race, and calendar year. Estimates were derived from interpolating the US Decennial Life Tables from the National Center for Health Statistics (NCHS) into individual years for the years 1970 through 2000 and from the US Annual Life Tables from NCHS for the years 2001 through 2009. Although the effect of deaths due to cervical cancer is also included in the life tables, this does not affect the estimated survival of the populations.[23,24] After matching, relative survival models were developed using annual intervals in the framework of generalized linear models with a Poisson error structure.[25-27] When modeling relative survival, the model is an additive hazards model where the total hazard is the sum of the baseline hazard from the control and the excess hazard associated with a diagnosis of cervical cancer. The exponentiated parameter

TABLE 1
Characteristics of patients with cervical cancer

	Stage I		Stage II		Stage III		Stage IV	
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
No.	26,337	(56.1)	7091	(15.1)	8090	(17.2)	5414	(11.5)
Age at diagnosis, y								
<50	18,023	(68.4)	3045	(42.9)	3943	(48.7)	1965	(36.3)
50–59	3770	(14.3)	1579	(22.3)	1747	(21.6)	1276	(23.6)
60–69	2534	(9.6)	1194	(16.8)	1135	(14.0)	1044	(19.3)
70–79	1388	(5.3)	797	(11.2)	799	(9.9)	709	(13.1)
≥80	622	(2.4)	476	(6.7)	466	(5.8)	420	(7.8)
Race								
Black	3485	(13.2)	1262	(17.8)	1448	(17.9)	990	(18.3)
White	22,852	(86.8)	5829	(82.2)	6642	(82.1)	4424	(81.7)
Year of diagnosis								
1983 through 1990	4671	(17.7)	1272	(17.9)	840	(10.4)	669	(12.4)
1991 through 2000	8982	(34.1)	2214	(31.2)	2418	(29.9)	1564	(28.9)
2001 through 2009	12,684	(48.2)	3605	(50.8)	4832	(59.7)	3181	(58.8)

Wright. Relative survival for cervical cancer. Am J Obstet Gynecol 2015.