Gynecologic Oncology 138 (2015) 421–428

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Long-term mortality among women with epithelial ovarian cancer☆

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HIGHLIGHTS

- The probability of dying from ovarian cancer decreases with time.
- Ovarian cancer remains the most common cause of death for 15 years after diagnosis in women with stage III–IV tumors.
- For stage I tumors, ovarian cancer remains the most common cause of death for 6 years after diagnosis.

ARTICLE INFO

Article history:
Received 20 May 2015
Received in revised form 2 June 2015
Accepted 3 June 2015
Available online 5 June 2015

Keywords:
Ovarian cancer
Survival
Surveillance
Cytoreduction
Debulking

ABSTRACT

Objectives. Patients with solid tumors are at greatest risk for dying from their cancers in the five years following diagnosis. For most malignancies, deaths from other chronic diseases begin to exceed those from cancer at some point. As little is known about the causes of death among long-term survivors of ovarian cancer, we examined causes of death by years from diagnosis.

Methods. The Surveillance, Epidemiology, and End Results (SEER) database was used to identify women diagnosed with ovarian cancer between 1988 and 2012. We compared causes of death by stage, age, and interval time after diagnosis.

Results. A total of 67,385 women were identified. For stage I neoplasms, 13.6% (CI, 13.0–14.2%) died from ovarian cancer, 4.2% (CI, 3.8–4.5%) from cardiovascular disease, 3.6% (CI, 3.3–3.9%) from other causes and 2.6% (CI, 2.4–2.9%) from other tumors; ovarian cancer was the leading cause of death until 7 years after diagnosis after which time deaths are more frequently due to other causes. For those with stage III–IV tumors, 67.8% (CI, 67.3–68.2%) died from ovarian cancer, 2.8% (CI, 2.6–2.9%) from other causes, 2.3% (CI, 2.2–2.4%) from cardiovascular disease and 1.9% (CI, 1.7–2.0%) from other cancers; ovarian cancer was the most frequent cause of death in years 1–15 after which time deaths were more commonly due to other causes.

Conclusions. The probability of dying from ovarian cancer decreases with time. Ovarian cancer remains the most common cause of death for 15 years after diagnosis in women with stage III–IV tumors.

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1. Introduction

There will be an estimated 21,290 cases of ovarian cancer diagnosed in the United States in 2015, which will result in approximately 14,180 deaths. Ovarian cancer has the lowest five year survival rate among gynecologic cancers at 46% [1]. Ovarian cancer typically remains asymptomatic in its early stages, and over 70% of patients present with advanced stage disease [2–5]. Women with early stage tumors typically respond well to treatment and some sub-groups have greater than 90% five-year survival rates. In contrast, five-year survival is less than 50% for patients with advanced stage disease [6].

For most solid tumors, the most common cause of death in the first five years after a diagnosis of cancer is due to cancer itself. As the duration from diagnosis increases, other causes of death become more common [7–9]. These findings have been reported for cancers of

☆ Dr. Wright (NCI R01CA169121-01A1) and Dr. Hershman (NCI R01 CA166084) are recipients of grants and Dr. Tergas is the recipient of a fellowship (NCI R25 CA094061-11) from the National Cancer Institute.

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http://dx.doi.org/10.1016/j.ygyno.2015.06.005
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the prostate [10,11], kidney [7], central nervous system [7,12–15], lung [11,16], head and neck [8], and colon [11,17]. In a study of 217,573 patients with breast, colorectal, lung, and prostate cancers, the probability of long-term survival increased significantly after patients survived a critical time period following diagnosis. The median conditional survival, or likelihood of survival after a specified time from initial diagnosis, increased from initial diagnosis to five years after diagnosis from 18.5 to 42.5 months for breast, 7.5 to 71.5 months for colorectal, 4.5 to 52.5 months for lung, and 24.5 to 34.5 months for prostate cancer [11].

Mortality estimates and the specific causes of death are of clinical importance to patients and physicians and can be used for counseling and prognostication as well as to help design more tailored surveillance and survivorship strategies [7,12,13,15,18,19]. In contrast to other solid tumors, little is known about the causes of death among long-term survivors of ovarian cancer. We therefore examined survival and cause of death among ovarian cancer patients and estimated the risk of death from various causes based on the duration since diagnosis.

2. Materials and methods

2.1. Data source

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database was utilized for this analysis [20,21]. SEER is a population-based cancer registry that includes data on approximately 28% of the United States population and captures patient demographics, cancer site and stage, and survival. Exemption from the Columbia University Institutional Review Board was obtained.

2.2. Patient characteristics

Women diagnosed with epithelial ovarian cancer between January 1988 and December 2012 were analyzed. The cohort was limited to women with epithelial ovarian tumors based on the World Health Organization (WHO) criteria including serous, mucinous, endometrioid, clear cell, transitional cell carcinomas, and epithelial tumors not otherwise specified [22]. Age at diagnosis was categorized into 10-year intervals, race recorded as white, black, and other, and diagnosis stratified by year. The SEER marital status variable was recorded as married, single, and unknown. The SEER registries were categorized as Eastern (Connecticut, New Jersey, Atlanta, rural Georgia, greater Georgia), Central (Detroit, Iowa, Kentucky, Louisiana, Utah), and Western (Alaska, California, Hawaii, Los Angeles, New Mexico, San Francisco, San Jose, Seattle). Tumor grade was grouped as well, moderately, or poorly differentiated, or unknown. Stage was determined based on the American Joint Cancer Committee and FIGO staging criteria as classified by SEER.

2.3. Outcomes

The primary outcome of the analysis was death. SEER records cause of death based on death certificate data. Patients were considered to have died from ovarian cancer if the cause of death was reported as ovarian cancer or cancer-related death likely due to ovarian cancer (miscellaneous malignant cancer, female genital tract cancer, cancer of the peritoneum, mesentery or omentum). Additional categories for cause of death included cardiovascular disease (disease of heart, hypertension without heart disease, cerebrovascular diseases, atherosclerosis, aortic aneurysm and dissection), other chronic disease (diabetes mellitus, Alzheimer's disease, chronic obstructive pulmonary disease and allied conditions, chronic liver disease and cirrhosis, nephritis, nephrotic syndrome and nephrosis), and other cancer ("all malignant cancers" with the exception of ovarian cancer). A category of other

Table 1
Clinical and demographic characteristics of the cohort.

	N	(%)
Year of diagnosis		
1988	1295	(1.9)
1989	1293	(1.9)
1990	1294	(1.9)
1991	1340	(2.0)
1992	1820	(2.7)
1993	1858	(2.8)
1994	1745	(2.6)
1995	1773	(2.6)
1996	1758	(2.6)
1997	1811	(2.7)
1998	1833	(2.7)
1999	1859	(2.8)
2000	3871	(5.7)
2001	3900	(5.8)
2002	3730	(5.5)
2003	3681	(5.5)
2004	3636	(5.4)
2005	3544	(5.3)
2006	3663	(5.4)
2007	3589	(5.3)
2008	3645	(5.4)
2009	3606	(5.4)
2010	3643	(5.4)
2011	3568	(5.3)
2012	3630	(5.4)
Age		
<40	3991	(5.9)
40–49	9663	(14.3)
50–59	15,489	(23.0)
60–69	16,248	(24.1)
70–79	13,934	(20.7)
≥80	8060	(12.0)
Race		
White	57,387	(85.2)
Black	4689	(7.0)
Other	5173	(7.7)
Unknown	136	(0.2)
Marital status		
Married	34,469	(51.2)
Single	30,587	(45.4)
Unknown	2329	(3.5)
Histology		
Serous	33,848	(50.2)
Mucinous	5729	(8.5)
Endometrioid	8280	(12.3)
Clear cell	4166	(6.2)
Transitional cell	264	(0.4)
Not otherwise specified	15,098	(22.4)
Grade		
Well differentiated	5270	(7.8)
Moderately differentiated	10,884	(16.2)
Poorly differentiated	30,929	(45.9)
Unknown	20,302	(30.1)
Region		
West	34,292	(50.9)
Central	16,029	(23.8)
East	17,064	(25.3)
Stage		
IA	8100	(12.0)
IB	764	(1.1)
IC	4871	(7.2)
INOS	455	(0.7)
II	5302	(7.9)
IIIA	1205	(1.8)
IIIB	1791	(2.7)
IIIC	16,275	(24.2)
IIINOS	5923	(8.8)
IV	19,465	(28.9)
Unknown	3234	(4.8)

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