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Epidemiology and outcomes of squamous ovarian carcinoma; a population-based study

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HIGHLIGHTS

- Squamous ovarian carcinoma is a very rare ovarian cancer with an unclear management.
- Patients usually present with disease confined to one ovary or loco-regional spread.
- Lymphadenectomy but not adjuvant radiotherapy is associated with improved survival.

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ABSTRACT

Objective. Squamous ovarian carcinoma (SOC) is a rare tumor. Scarcity of information about the epidemiology and prognosis of SOC hinders attempts at optimal patient management. This retrospective study of a large cohort details the clinicopathological and demographic characteristics and prognosis of women with SOC.

Methods. A cohort of patients drawn from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database who were diagnosed with SOC between 1988 and 2012 were analyzed. Observed and disease-specific survival was estimated by Kaplan-Meier plots in women who underwent surgery as part of their cancer-related treatment. A Cox hazard regression analysis was performed to determine independent predictors of cancer-specific survival in patients with SOC.

Results. We identified 341 patients with SOC with a median age at diagnosis of 55 years. Stage I, II, III and IV tumors were noted in 34%, 15%, 20.5% and 24.9% of patients, respectively. Five-year cancer-specific survival was 86% for stage I, 54.3% for stage II, 36.3% for stage III and 2.8% for stage IV disease patients. Observed and cancer-specific survival was better for patients that underwent lymphadenectomy ($p = 0.031$). Postoperative radiotherapy was not associated with improved survival. In a multivariate analysis, independent predictors of improved cancer-specific survival were younger age, lower disease stage and lymphadenectomy.

Conclusions. SOC is typically a unilateral malignancy with a tendency toward loco-regional spread. Stage I patients have a relatively high survival rate; however, the prognosis is poor for women with abdominal or distant spread. Lymphadenectomy, but not postoperative radiotherapy, is associated with improved survival.

1. Introduction

Ovarian cancer is currently the 8th most common malignancy among women in the United States with an annual incidence of 20,785 cases [1]. During the last decade, knowledge of ovarian cancer pathophysiology has drastically expanded due to significant advances in histological, cellular and molecular laboratory techniques [2]. Ovarian cancer is a heterogeneous group of tumors of different histological type, each associated with distinct epidemiological and clinical features and accompanied by a variable prognosis [3].

Squamous ovarian carcinoma (SOC) is a rare tumor, representing <1% of all ovarian malignancies [4]. The majority of these tumors arise from malignant transformation of ectodermal tissue found within a mature cystic teratoma [4]. Less frequently, SOC can derive from malignant transformation of endometriotic foci or a benign Brenner tumor [5]. SOC arising de novo from the ovarian surface epithelium is extremely uncommon [6].

Two overlapping systematic reviews summarized data derived from 220 and 277 cases of SOC, respectively [7,8]. However, a larger study on the epidemiology and prognosis of SOC is warranted to guide the optimal management of these patients. In this population-based study we

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investigated the clinicopathological and demographic characteristics and prognosis of women with SOC.

2. Material methods

We analyzed a cohort of patients drawn from the National Cancer Institute's SEER database [9]. The SEER database captures data such as patient demographics, primary tumor site, histology, tumor grade and morphology, initial staging, treatment, and follow-up of patient status. Rigorous quality control ensures the collection of highly reliable data. In the present study, we included 18 cancer registries (Detroit, Iowa, Kentucky, Louisiana, Utah, Connecticut, New Jersey, Atlanta, Rural and Greater Georgia, Alaska, California, Hawaii, Los Angeles, New Mexico, San Francisco, San Jose, Seattle), as released on November 2014, which cover approximately 27.8% of the total US population based on the 2010 census [10]. SEER database is available for public use and all patient data are de-identified; an exemption was also granted from obtaining institutional review board approval.

Inclusion criteria used to identify eligible patients were: (1) tumors with malignant behavior located at the ovary (ICD-O-3/WHO 2008 site code C.569) [11], (2) tumors of squamous histology, (3) tumor diagnosis between January 1, 1988 and December 31, 2012 and (4) diagnosis not obtained from autopsy or death certificate.

The following histological ICD-O-3 codes were employed: 8052 (papillary squamous carcinoma), 8070 (squamous cell carcinoma, NOS), 8071 (squamous cell carcinoma, keratinizing NOS), 8072 (squamous cell carcinoma, large cell, non-keratinizing), 8073 (squamous cell carcinoma, small cell, non-keratinizing), 8074 (squamous cell carcinoma, spindle cell) and 8084 (squamous cell carcinoma, clear type). We opted not to include the histological code 8050 (papillary carcinoma, NOS) in our analysis because contrary to other sites (e.g. esophagus, cervix) at the ovary this code is highly likely to include cases of papillary adenocarcinomas.

Demographic (age at tumor diagnosis, race, year of diagnosis, marital status and geographic area of residency at time of diagnosis) and clinico-pathological parameters (tumor grade, laterality, stage, number of lymph nodes examined, details on treatment, survival and cause of death) were extracted using the "case listing" option. Based on previous studies registries were grouped as followed: central (Detroit, Iowa, Kentucky, Louisiana, Utah), eastern (Connecticut, New Jersey, Atlanta, Rural and Greater Georgia) and western (Alaska, California, Hawaii, Los Angeles, New Mexico, San Francisco, San Jose, Seattle) [12]. Tumor staging was based on the 7th edition of the American Joint Committee on Cancer (AJCC) staging system for patients diagnosed in 2010–2012, the 6th edition of the AJCC staging for 2004–2009 and the SEER-modified 3rd edition of AJCC staging for patients diagnosed between 1988 and 2003 as in previous analysis [13]. In addition we extracted SEER-derived historical stage.

Observed and disease-specific survival was estimated in a subcohort of women who underwent surgery as part of their cancer-related treatment. In addition, to estimate disease-specific survival we included only patients diagnosed with a first primary malignant tumor; those who died from causes other than ovarian cancer were censored. Patients were presumed alive at the time of study cut-off (December 31st, 2012). In the SEER database, survival is calculated as the number of months from cancer diagnosis to the date of death. To determine survival rates, Kaplan-Meier curves were generated. Comparisons of survival between different groups were made using the log-rank test. A Cox hazard regression analysis was also employed to determine independent predictors of disease-specific survival of patients with SOC. Factors entered into a multivariate model were age and geographic residency at diagnosis, race, marital status, tumor stage, grade and lymphadenectomy. Statistical analysis was performed with the SPSS version 22 statistical package. The alpha level of statistical significance was set at 0.05 and all p-values were two-sided.

Table 1
Demographic and clinicopathological characteristics of SOC patients.

	n (%)
Age at diagnosis	
<50	117 (34.3%)
50–64	113 (33.1%)
65–74	57 (16.7%)
≥75	54 (15.8%)
Race	
White	257 (75.4%)
Black	41 (12%)
Other/unknown	43 (12.6%)
Marital status	
Married	172 (50.4%)
Single	156 (45.7%)
Unknown	13 (3.8%)
SEER registry	
Eastern	85 (24.9%)
Central	89 (26.1%)
Western	167 (49%)
Year of diagnosis	
1988–1992	30 (8.8%)
1993–1997	40 (11.7%)
1998–2002	64 (18.8%)
2003–2007	87 (25.5%)
2008–2012	120 (35.2%)
Tumor grade	
Unknown	91 (26.7%)
Available	250 (73.3%)
Grade I	25 (10%)
Grade II	83 (33.2%)
Grade III	133 (53.2%)
Grade IV	9 (3.6%)
Laterality	
Unilateral	276 (80.9%)
Bilateral	27 (7.9%)
Unknown	38 (11.2%)
Stage (historic)	
Localized	113 (33.1%)
Regional	66 (19.4%)
Distant	151 (44.3%)
Unstaged	11 (3.2%)
Stage (AJCC)	
I	116 (34%)
IA	82 (24%)
IB	4 (1.2%)
IC	25 (7.3%)
INOS	5 (1.5%)
II	51 (15%)
IIA	9 (2.6%)
IIB	29 (8.5%)
IIC	10 (2.9%)
IINOS	3 (0.9%)
III	70 (20.5%)
IIIA	5 (1.5%)
IIIB	6 (1.8%)
IIIC	44 (12.9%)
IIINOS	15 (4.4%)
IV	85 (24.9%)
Unknown	19 (5.6%)
Surgery performed	296 (86.8%)
Lymphadenectomy	
Yes	147 (43.1%)
No	182 (53.4%)
Unknown	12 (3.5%)
Status of examined regional lymph nodes	
Positive	40 (27%)
Negative	108 (73%)
Radiation therapy	51 (15%)

3. Results

We identified 341 patients with SOC that met our inclusion criteria. The median age of patients was 55 years; 67.4% were younger than 65. At diagnosis, stage I and IV tumors were noted in 34% and 24.9% of