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Adherence to treatment recommendations and outcomes for women with ovarian cancer at first recurrence☆,☆☆

Miriam Champer [a], Yongmei Huang [a], June Y. Hou [a,b,c], Ana I. Tergas [a,b,c,d], William M. Burke [a,b,c], Grace Clarke Hillyer [d], Cande V. Ananth [a,d], Alfred I. Neugut [a,b,c,d], Dawn L. Hershman [a,b,c,d], Jason D. Wright [a,b,c,*]

[a] Columbia University College of Physicians and Surgeons, United States
[b] Herbert Irving Comprehensive Cancer Center, United States
[c] New York Presbyterian Hospital, United States
[d] Mailman School of Public Health, Columbia University, United States

HIGHLIGHTS

- Platinum free interval is a strong predictor of survival in elderly women with recurrent ovarian cancer.
- There is widespread variation in treatment selection for women with recurrent ovarian cancer.
- Many women receiving non-guideline based regimens.

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ABSTRACT

Objective. Treatment selection for recurrent ovarian cancer is typically based on the duration of time between the completion of adjuvant, platinum-based therapy and the time of recurrence, the platinum free interval (PFI). We examined the use of, and outcomes associated with platinum-based chemotherapy based on the PFI in women with recurrent ovarian cancer.

Methods. The Surveillance, Epidemiology, and End Results-Medicare database was used to identify women aged >65 years with epithelial ovarian cancer who underwent surgery and platinum-based chemotherapy and who developed a recurrence >3 months after the completion of adjuvant therapy. Patients were stratified by PFI into 3 groups: PFI <6 months, PFI 7–12 months, and PFI >12 months. Multivariable models were used to examine predictors of use of platinum-based therapy and survival for each group.

Results. A total of 2369 patients were identified. In women with a PFI of ≤6 months, treatment consisted of platinum-based combination therapy in 28.2%, single agent platinum in 5.2% and non-platinum therapy in 66.6%. Corresponding rates of these treatments among women with a PFI of 7–12 months were 39.7%, 12.4% and 47.9%, respectively; the rates were 57.6%, 13.2% and 29.3% in those with a PFI of >12 months, respectively. Median survival was 13, 18, and 27 months for patients with a PFI of ≤6 months, 7–12 months, and >12 months, respectively ($P < 0.0001$). For all three groups, platinum combination therapy was associated with decreased risk of death compared to non platinum based therapy.

Conclusion. Platinum free interval is a strong predictor of survival in elderly women with recurrent ovarian cancer. There is widespread variation in treatment selection for women with recurrent ovarian cancer with many women receiving non-guideline based regimens.

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* Corresponding author at: Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons, 161 Fort Washington Ave, 4th Floor, New York, NY 10032, United States.
E-mail address: jw2459@columbia.edu (J.D. Wright).

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1. Introduction

Despite a high initial response rate to surgery and chemotherapy, women with ovarian cancer are at significant risk for recurrence following primary treatment. Among patients with early-stage ovarian cancer, 25% will have a recurrence, and 80% of patients with advanced disease will recur [1]. A wide variety of cytotoxic and biologic agents are now available for the treatment of women with recurrent ovarian cancer [2–4].

Treatment selection for recurrent ovarian cancer is typically based on the duration of time between the completion of adjuvant platinum-based therapy and the time of recurrence, the so-called platinum free interval (PFI) [5,6]. Those women who have a short PFI are less likely to respond to retreatment with platinum-based therapy, while patients with a longer PFI are more likely to respond [7]. The PFI is also an important prognostic factor; a longer PFI is associated with improved survival [8].

Women with recurrent ovarian cancer and a PFI of ≤6 months are typically classified as platinum resistant and recommendations are for treatment with non platinum based chemotherapy. Those women with a PFI of >6 months are considered to have platinum sensitive disease and treatment recommendations generally encourage retreatment with platinum-based therapy, usually platinum-based combination therapy. Patients with a long PFI (>12 months) have the highest response rate to platinum retreatment and thus the strongest rationale for receiving such therapy [5,9].

Despite the availability of treatment recommendations for women with recurrent ovarian cancer based on PFI, little is known about the actual patterns of care for women with ovarian cancer in the general population. We performed a population-based analysis in elderly women with recurrent ovarian cancer to determine the use and outcomes of platinum-based chemotherapy based on clinical characteristics and the length of the platinum free interval.

2. Methods

2.1. Data source

We used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database for the analysis [10–16]. The SEER program is a population-based tumor registry maintained by the National Cancer Institute that currently covers approximately 28% of the US population [17]. SEER captures data on date of cancer diagnosis, tumor histology, location, stage, treatment, and survival, as well as demographic and selected census tract-level information. Using a matching algorithm, 93–94% of SEER patients diagnosed at age 65 or older are linked to Medicare health care claims [18,19]. The Medicare claims database captures information on patients with Medicare part A (inpatient) and part B (outpatient), including billed claims, services, and diagnoses. These two files are linked and provide data on initial services and all follow-up care longitudinally. Exemption from the Columbia University Institutional Review Board was obtained.

2.2. Cohort selection

Women aged 65 years or older with epithelial ovarian cancer were selected. Patients who were diagnosed between January 1, 1992 and December 31, 2009, and received cancer directed surgery from one month before to within 6 months of diagnosis were included. The cohort was limited to women who underwent surgery for ovarian cancer and received combination platinum- and taxane-based chemotherapy after surgery. Patients may have received preoperative (neoadjuvant) chemotherapy in addition to postoperative chemotherapy. Patients who received adjuvant chemotherapy for >8 months were excluded. The study specifically focused on treatment of women with recurrent ovarian cancer. We therefore selected patients who initiated second line chemotherapy ≥3 months after completion of adjuvant treatment. Patients with incomplete claims, such as those who enrolled in a non-Medicare health maintenance organization, those receiving Medicare for a reason other than age, and patients with other primary cancers were excluded (Fig. 1).

2.3. Patient characteristics

Age at diagnosis was stratified into 5-year intervals and race was recorded as white, black, and other. Marital status was recorded as married, not married, and unknown. An aggregate socioeconomic status (SES) score was calculated from education, poverty level, and income information from the 2000 census tract data, as previously reported by Du and co-workers [20]. The SES scores were ranked on a scale of 1–5 by use of the formula that incorporated education, poverty, and income weighted equally, with 1 being the lowest value. The prevalence of comorbid medical diseases was assessed using the Klabunde adaptation of the Charlson comorbidity index (ie, the Klabunde–Charlson index) [21,22]. Medicare claims were examined for diagnostic codes of the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). Each condition was weighted, and patients were assigned a score that was based on the Klabunde–Charlson index [22]. Area of residence was categorized as metropolitan or nonmetropolitan. The SEER registries were grouped as: Eastern, Western and Midwest. Stage was captured using the American Joint Cancer Commission staging criteria. Tumor histology was classified as serous, mucinous, endometrioid, clear cell or other. Tumor grade was grouped as well [1], moderately [2] or poorly differentiated, [3] or unknown.

2.4. Treatment and outcomes

To identify ovarian cancer directed surgery and chemotherapy use, we extracted claims from the Medicare files by searching the Level II Healthcare Common Procedure Coding System codes, Current Procedural Terminology (CPT) codes, and ICD-9-CM diagnostic and procedure codes from Medicare provider and analysis review files, physician claims files, and the hospital outpatient claims files. In addition, revenue center codes were also added when querying chemotherapy data. Cancer directed surgery included any procedure claims for oophorectomy, hysterectomy, oophorectomy and debulking, exenteration, or debulking from 1 month before to 6 months after cancer diagnosis.

If a patient had any chemotherapy claims prior to cancer directed surgery, she was coded as having received neoadjuvant chemotherapy. If a patient had at least one claim for chemotherapy within 90 days of surgery, she was coded as having received postoperative chemotherapy. The duration of initial chemotherapy was calculated from the date of first chemotherapy claim after surgery through the date of last claim without a break of >3 months between any two claims. The duration of adjuvant chemotherapy was classified as 1–4, 5–6, and 7–8 months. If a patient had any chemotherapy claims at 3 or more months after the completion of first treatment, she was coded as having received second course of chemotherapy post-surgery. The interval from first to second chemotherapy course (platinum free interval, PFI) was categorized as ≤6, 7–12, and >12 months. The second course of chemotherapy was classified as single agent platinum if cisplatin, carboplatin or oxaliplatin were used alone. If a second agent was given concurrently, the patient was classified as having received platinum combination therapy. Receipt of any non platinum containing single or multiagent regimen was considered as non platinum chemotherapy. The primary outcome was survival. Survival was measured as the time from initiation of the second chemotherapy to death from any cause.

2.5. Statistical analysis

Frequency distributions between categorical variables were compared using χ^2 tests or Fisher's exact test. Multivariable log-linear