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Cost-Utility Analysis of Platinum-Based Chemotherapy versus Taxane and Other Regimens for Ovarian Cancer

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ABSTRACT

Objectives: Most economic evaluations of chemotherapies for ovarian cancer patients have used hypothetical cohorts or randomized control trials, but evidence integrating real-world survival, cost, and utility data is limited. **Methods:** A propensity score–matched cohort of 6856 elderly (≥65 years) ovarian cancer patients diagnosed from 1991 to 2005 from the Surveillance, Epidemiology, and End Results-Medicare data cohort were included. Treatment regimens (i.e., no chemotherapy, platinum-based only, platinum plus taxane, and other nonplatinum) were identified in the 6 months postdiagnosis. Patients were followed until death or end of study (December 2006). Effectiveness was measured in quality-adjusted life-years (QALYs), and total health care costs were measured by using a payer's perspective (2009 US dollars). Methodological and statistical uncertainties were accounted by including alternative scenarios (for utility values) and net monetary benefit approach. Incremental cost-effectiveness ratios (ICERs) were calculated, and stratified analyses were performed by tumor stages and age groups. **Results:** On comparing the platinum-based group versus no chemotherapy, we found that the ICER was $30,073/QALY and $58,151/QALY for early- and late-stage disease, respectively, while other nonplatinum and platinum plus taxane groups were dominated (less effective and more costly). Similar results were found across alternative scenarios and age groups. For patients 85 years or older, platinum plus taxane, however, was not dominated by the platinum-based group, with an ICER of $133,892/QALY. **Conclusions:** Following elderly ovarian cancer patients over a lifetime using real-world longitudinal data and adjusting for quality of life, we found that treatment with platinum-based regimen was the most cost-effective treatment alternative.

Keywords: chemotherapy, cost-effectiveness, cost-utility, ovarian cancer.

Introduction

The primary treatment for women with early-stage ovarian cancer is surgical resection/tumor debulking followed by systemic chemotherapy. For patients with stage IA or IB and grade I ovarian cancer, observation is recommended after surgery because of the high cure rate for these patients with surgery alone. Controversy remains regarding the potential benefit of adjuvant chemotherapy for patients with stage IA and grade II tumors; the National Institutes of Health consensus expert panel has reported that either observation or chemotherapy is an appropriate recommendation [1–3]. For patients with higher grade tumors and/or more advanced stages of disease, systemic chemotherapy is recommended [1–3]. Platinum and taxane combination is the recommended primary therapy for cancer stages IC to IV, while single agents may be administered depending on the platinum sensitivity of the tumor [2]. We recently reported chemotherapy effectiveness results from a national study of 12,181 patients aged 65 years and older diagnosed with stages I to IV ovarian cancer and treated from 1991 to 2005 [4]. Platinum and taxane combination therapies and platinum-based therapies without taxane yielded an increased survival, including a significant dose-response effect among patients with late-stage cancer. For patients with early-stage ovarian cancer, platinum and taxane combination therapy was more effective than other chemotherapy treatments. Combination therapy, however, had higher toxicity, which was consistent with clinical trial findings. Survival was poor among patients initially diagnosed with late-stage cancer, regardless of chemotherapy treatment.

While survival is of primary importance, there are concerns about decreasing effectiveness of chemotherapy in an aging population, the effects of toxicity on quality of life, and the cost-effectiveness of alternative treatments. While clinical trials have shown that the efficacy of adjuvant chemotherapy for breast cancer decreases with age [5–8], currently no evidence shows decreasing efficacy of chemotherapy with age for ovarian

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cancer [9–14]. There are model-based cost-effectiveness studies [15–19] of alternative ovarian cancer chemotherapy regimens, but none was on a national population of community-based patients and providers, incorporating quality of life, or investigating cost-effectiveness of treatments as patients age. Furthermore, previous ovarian cancer cost-effectiveness studies have focused on individual drugs, administration route, and treatment frequency [15–19]. Most studies derive effectiveness from clinical trials with a limited time horizon [18,20–22]. Empirical studies included patients with a mean age of 60 years and a maximum age of 85 years [15,19,23,24]. In randomized clinical trials, the combination of cisplatin and paclitaxel has been shown to be a cost-effective first-line therapy [15,19,24,25]. Among platinum-sensitive recurrent patients, carboplatin and paclitaxel therapy was cost-effective as compared with carboplatin alone or other platinum-based therapies [18,21]. For example, Havrilesky et al. [18] found an incremental cost-effectiveness ratio (ICER) of $15,564 per progression-free life-year for carboplatin and paclitaxel versus an ICER of $278,388 for carboplatin and gemcitabine.

We used a large national Surveillance, Epidemiology, and End Results (SEER)-Medicare data set to examine whether common chemotherapy regimens for women with ovarian cancer remained effective as women age, and which chemotherapy regimens were cost-effective and offered the highest quality-adjusted survival. The study complements randomized clinical trials and modeling studies of ovarian cancer and further informs decision makers who are concerned about the economic and clinical consequences of cancer treatment in an aging population. The methodology and novelty of the approach to real-world population-based patient data can be applied to answer similar questions for patients with other tumors and serve as a reference to other investigators.

Methods

Data Source, Population, and Chemotherapy Regimens

A retrospective cohort study was conducted by using the SEER and Medicare linked database. Additional information on SEER and SEER-Medicare linkage is described in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.11.007. Women diagnosed with ovarian cancer as the first primary tumor without other primary tumors at age 65 years or older from January 1, 1991, to December 31, 2005 [4], were considered for the study. A total of 12,181 women with American Joint Committee on Cancer stages I to IV or unknown stage at diagnosis were identified from 16 SEER areas. Patients with American Joint Committee on Cancer stage IA or IB were included in the study because some received chemotherapy and the National Institutes of Health consensus expert panel felt that either observation or chemotherapy is appropriate [1–3]. Patients were considered to have received chemotherapy if associated codes (see Supplemental Materials) were identified within 180 days after diagnosis in Medicare claims. Chemotherapy regimens were defined by using HCPCS codes J9045, J9060, J9062, and J9263 for platinum-based drugs and J9170 and J9265 for taxanes. Propensity scores (conditional probability) were computed for the receipt of platinum-based chemotherapy as compared with the receipt of other nonplatinum chemotherapy or no chemotherapy, while adjusting for age, ethnicity, marital status, tumor stage, grade, size, number of positive lymph nodes, comorbidity, surgery, radiation therapy, socioeconomic status, and year of diagnosis. A one-to-one match was performed on the basis of the above-obtained propensity scores by using the 5-1 digit validated matching algorithm [26]. The matched sample comprised 6856 ovarian cancer patients (3428 each in platinum-based chemotherapy and nonplatinum/no chemotherapy group). Patients were then hierarchically grouped into four categories: no chemotherapy, other nonplatinum chemotherapy, only platinum-based chemotherapy, and platinum plus taxane chemotherapy. Platinum plus taxane categorization required both platinum and taxane claims within 141 days, accommodating six cycles of 3 weeks each and an additional 15-day grace period. Plots of propensity score distribution across all four groups of patients showed considerable overlap, suggesting them to be comparable (see Fig. 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.11.007.

Effectiveness

Effectiveness was measured as quality-adjusted life-years (QALYs), obtained by adjusting overall survival with phase-, stage-, and adverse event–specific utilities. Overall survival benefits were calculated by following patients from the start of treatment to death or end of study (December 31, 2006). Survival time after treatment initiation was distributed into initial, continuing, and terminal phases (see Fig. 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.11.007). The initial and terminal phases were the first and last 6 months of life, respectively, while the continuing phase was the time between initial and terminal phases. Patients alive at the end of the study were not assigned terminal phase time. Patients surviving less than 6 months were assigned only to the terminal phase, and patients surviving less than a year had the last 6 months assigned to the terminal phase and the remainder to the initial phase [27].

Utility weights were obtained from the existing literature and were assigned to each phase [28,29]. Base-case and alternative (best-case and worst-case) scenario utility weights are listed in Table 1. During the initial phase, patients categorized in the "no chemotherapy" group were assigned a diagnosis stage–specific utility ("early ovarian cancer" and "advanced ovarian cancer"). Patients who received some chemotherapy during the initial phase were given a utility weight associated with "chemotherapy/grade 1/2 toxicity." Adverse events identified from inpatient Medicare claims were considered grade 3/4 adverse events and were assigned a utility weight associated with "chemotherapy/grade 3/4 toxicity." Adverse events identified by using *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes included alopecia, nausea/vomiting, fatigue, neutropenia, myalgia/pain, stomatitis, and peripheral neuropathy [30].

In the continuing phase, patients were assigned the average of utilities associated with "remission" and "progression." A "terminal cancer" utility was applied to the terminal phase. For the time between diagnosis and start of the initial phase, stage-specific utilities were applied. Finally, individual phase-specific QALYs were obtained by multiplying the time spent in that phase with the associated utility weight. Total QALYs for each patient were obtained by summing all phase-specific QALYs and were discounted by 3% annually [31].

Cost Analysis

Health care costs were estimated from a payer perspective, using the amount Medicare paid for each claim. Because cancer treatments may affect the overall morbidity, total health care costs were calculated including inpatient services, outpatient visits and procedures, physician fees, skilled nursing facility, hospice, and costs for devices and medical equipment from the start of treatment until death or end of study. Costs were aggregated by phase by using criteria similar to that for distributing QALYs. Cost data were aggregated over a 16-year period (1991–2006) and from various geographical locations, necessitating adjustment for inflation and the cost of doing business, respectively [32]. Brown