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Review article

Ovarian cancer in the older woman

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ABSTRACT

Ovarian cancer is the seventh most common cancer in women worldwide and accounts for nearly 4% of all new cases of cancer in women. Almost half of all patients with ovarian cancer are over the age of 65 at diagnosis, and over 70% of deaths from ovarian cancer occur in this same age group. As the population ages, the number of older women with ovarian cancer is increasing. Compared to younger women, older women with ovarian cancer receive less surgery and chemotherapy, develop worse toxicity, and have poorer outcomes. They are also significantly under-represented in clinical trials and thus application of standard treatment regimens can be challenging. Performance status alone has been shown to be an inadequate tool to predict toxicity of older patients from chemotherapy. Use of formal geriatric assessment tools is a promising direction for stratifying older patients on trials. Elderly-specific trials, adjustments to the eligibility criteria, modified treatment regimens, and interventions to decrease morbidities in the vulnerable older population should be encouraged.

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Contents

1. Introduction . . . 0
2. Geriatric Assessment . . . 0
   2.1. Background . . . 0
   2.2. Presurgery Assessment . . . 0
   2.3. Pre-chemotherapy Assessment . . . 0
   2.4. Surgery . . . 0
3. Chemotherapy . . . 0
   3.1. Background . . . 0
   3.2. Chemotherapy: 1st Line . . . 0
      3.2.1. European Studies . . . 0
      3.2.2. U.S. Studies . . . 0
      3.2.3. Neoadjuvant Chemotherapy (NACT) . . . 0
      3.2.4. Intraperitoneal Chemotherapy (IP) . . . 0
   3.3. Chemotherapy for Recurrent Disease . . . 0
   3.4. Targeted Agents . . . 0

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1. Introduction

Cancer is recognized as a disease of older adults, with over 50% of new cases being diagnosed after age 65, and over 70% of deaths from cancer occurring in this same age group.[1] Ovarian cancer is the seventh most common cancer in women worldwide and accounts for nearly 4% of all new cases of cancer in women.[2] It is also the eighth most common cause of cancer death in the world.

Almost 50% of ovarian cancer is diagnosed in women over the age of 65.[3] This ratio is expected to increase in the coming decades as our population ages and life-expectancy improves.[4,5] Outcomes steadily worsen as the age of the patient rises. One European report showed age-standardized relative survival rates at one year of 57% for women aged 65–69 years, 45% for those aged 70–74 years, and 33% for those aged 80–84 years.[6] There have been various theories put forward to account for the decreased survival in older women, including: (1) more aggressive cancer with advanced age, including higher grade and more advanced stage; (2) inherent resistance to chemotherapy of cancers occurring in older women; (3) individual patient factors such as multiple concurrent medical problems, polypharmacy, functional dependence, cognitive impairment, depression, frailty, poor nutrition, and limited social support leading to greater toxicity with therapy; and (4) physician and health care biases towards the elderly which lead to inadequate surgery, suboptimal chemotherapy, and poor enrollment in clinical trials.[7] Guidelines have been developed to help inform oncologists on caring for the older adult with cancer.[8] In this review, we will highlight the current evidence and research in treatment for women with ovarian cancer.

2. Geriatric Assessment

2.1. Background

Geriatric assessment (GA) provides clinicians with information about a patient's functional status, comorbid medical conditions, cognition, psychological status, social functioning-support, and nutritional status. In the cancer setting, several studies have demonstrated the predictive value of GA for estimating the risk of severe toxicity from chemotherapy and surgery.[9–11] There are several geriatric assessments reported and currently under study, specifically in women with gynecologic cancers. Briefly, these include the GINECO Geriatric Vulnerability Scale, the NRG preoperative score and the CARG assessment, and its similarly derived GOG Geriatric Assessment Score. These are discussed in more detail below and summarized in Table 1.

2.2. Presurgery Assessment

GA under study for breast and other solid tumors may be applicable to women with ovarian cancer; for example, the Preoperative Assessment of Cancer in the Elderly (PACE) tool was developed to combine elements of the comprehensive geriatric assessment with surgical risk assessment tools. The authors found no significant association of age with post-operative complications. IADL, Brief Fatigue Inventory (BFI), and Performance Status (PS) were most predictive of 30-day morbidity. Lower scores for Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), and performance status (PS) were associated with extended hospital stay.[12,13]

The American College of Surgeons released a position paper in 2012 outlining best practices for the optimal preoperative assessment of the geriatric patient.[14] In addition, the NRG-Oncology Cooperative Group recently completed a GA study in older women undergoing laparotomy for newly diagnosed ovarian cancer (NRG-CC002), both as primary and interval surgery after neoadjuvant chemotherapy. The study used a modification of the PACE tool to determine the benefit of a GA in predicting post-surgical complications. Accrual is completed and results are expected in 2016.

2.3. Pre-chemotherapy Assessment

The Cancer and Aging Research Group (CARG) Geriatric Assessment (GA) and Toxicity Score is one example of a short screening test to assess chemotherapy toxicity risk. CARG-GA predicted grades 3–5 chemotherapy toxicity far better than performance status.[11] The CARG study included a small proportion of women with ovarian cancer (50 patients, 10%) and a retrospective subgroup analysis showed that grades 3–5 toxicity occurred in 19 patients (37%). Compared to the CARG study (n = 500), the ovarian cancer cohort were similar in age (median 73), stage distribution (90% vs. 83% stages III–IV), and treatment with doublet chemotherapies (75% vs. 70%) at standard doses (65% vs. 76%). Abnormal CA125 (likely as a surrogate for disease burden) was associated with assistance with IADL, low PS, chemotherapy toxicity, and dose reductions.[15]

The French Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO) has developed a "Geriatric Vulnerability Score (GVS)" from a series of up-front trials in women with ovarian cancer who were 70 years or older and had advanced stages (III–IV). In a univariate analysis, FIGO stage IV, performance status ≥2, age older than 80, ADL < 6, IADL <25, 3 or greater comorbidities, albumin <35 g/L, and lymphocyte <1 G/L were all statistically associated with poor survival. The proposed GVS includes low albumin (<35 g/L), low ADL score (<6), low IADL score (<25), lymphopenia (<1 G/L), and a high Hospital Anxiety and Depression (HADS) score (>14).[16] With a cutoff score of 3, two groups of patients were identified. Compared with patients with a GVS score of 3 or higher, a lower score was associated with significantly worse overall survival (11.5 vs. 21.7 months; hazard ratio [HR] 2.94), lower rate of completion of chemotherapy (65% vs. 82%; odds ratio [OR]

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