Gynecologic Oncology 136 (2015) 136–142

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Review

Treatment of ovarian cancer in the older woman

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HIGHLIGHTS

- Older women with ovarian cancer have a worse survival than younger women.
- Older women with ovarian cancer get less chemotherapy and surgery for ovarian cancer and experience more toxicity.
- Geriatric Assessment Tools can help predict which older patients will have toxicity from therapy.

ARTICLE INFO

Article history:
Received 18 September 2014
Accepted 28 October 2014
Available online 3 November 2014

Keywords:
Ovarian
Geriatric
Elderly

ABSTRACT

Half of ovarian cancer patients are over the age of 65, and as the population ages, the number of older women with ovarian cancer is increasing. Older women with ovarian cancer receive less surgery and chemotherapy than younger women, suffer worse toxicity from surgery and chemotherapy than younger women, and have worse survival. Performance status has been shown to be an inadequate tool to predict toxicity of older patients from therapy. Use of formal geriatric assessment tools is a promising direction for stratifying older patients on trials. We review current data on outcomes with surgery and chemotherapy in the older population, and discuss geriatric assessment tools being studied to aid decisions regarding which older patients will tolerate standard therapy and which will not. Modified treatment regimens and interventions to decrease morbidities in the vulnerable older population should be useful.

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http://dx.doi.org/10.1016/j.ygyno.2014.10.028
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Background

About 50% of ovarian cancer is diagnosed in women over the age of 65 [1]. This ratio is expected to increase in the coming decades as our population ages and life-expectancy improves [2,3]. It is clear that, on average, 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 [4]. 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 and malnutrition 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 [5].

To improve the outcomes of our older women with ovarian cancer we will eventually have to better understand biologic differences between tumors of younger and older patients, but at this time we cannot well predict chemosensitivity of high grade serous tumors in women at any age. In the near term we need to develop better decision aids to discriminate those patients who will and will not tolerate standard cytoreductive surgery and chemotherapy. Our trials and reports cannot focus exclusively on the healthiest subsection of older women. We may need to modify chemotherapy dosing, scheduling, and timing (neoadjuvant or postoperative) to reduce toxicity in the more vulnerable patients. Finally, there is a need to develop interventions to improve the ability of vulnerable older women to undergo surgery and receive chemotherapy. In this review, we will discuss currently available data regarding results of surgery and chemotherapy in the older population as well as reviewing geriatric assessment tools being developed to aid decision-making regarding both surgical and chemotherapeutic interventions.

Geriatric assessment

Background

Geriatric assessment (GA) provides information about a patient's functional status (ie. ability to live independently at home and in the community), co-morbid 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 survival outcomes [6–8]. A validated instrument for assessment specifically for the older patient with ovarian cancer patient does not yet exist. There are several excellent assessments (Table 1) which may lend themselves to this unique population but further prospective studies are imperative to remove the guess work from assessing a patient's fitness for surgery or chemotherapy.

Presurgery assessment

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 (Table 1). The authors found no significant association of age with post-operative complications. IADL (Instrumental Activities of Daily Living; more complex activities such as managing finances and shopping), moderate to severely elevated scores on the Brief Fatigue Inventory (BFI) and abnormal Performance Status (PS) were most predictive of 30 day morbidity. Lower scores for Activities of Daily Living (ADL; basic activities such as eating, bathing, dressing), (IADL) and worse performance status (PS) were associated with extended hospital stay [9,10]. Of note, patients with gynecologic cancers were not included in development of the PACE tool (almost half had breast cancer). A position paper was released in 2012 by the American College of Surgeons outlining best practices for optimal preoperative assessment of the geriatric patient with a standard checklist. However no overall risk score is calculated [11]. The "Timed Up & Go" which assesses walking speed, has been reported to predict 30-day surgical morbidity in patients 70 years of age or older undergoing cancer surgery (61% of the operations involved laparotomy). This was part of the PREOP study which is designed to assess a number of different presurgical assessments in older patients with a variety of cancers undergoing a variety of different operations [12].

Prechemotherapy assessment

As with the presurgical assessment, there is clear need for a simple and short screening test to assess toxicity risk for older vulnerable women with ovarian cancer undergoing chemotherapy, and a variety have been/are being tested (Table 1). Examples of a short survey used in various cancers are the Vulnerable Elders Survey (VES-13) and the Cancer and Aging Research Group (CARG) Geriatric Assessment (GA) and Toxicity Score. VES-13 is a self-administered survey that consists of one question for age and 12 additional questions assessing self-rated health, functional capacity and physical performance. CARG-GA is a feasible assessment (mean time to completion is 27 min, mostly self-administered) and the 11-point summary score (Table 1) predicted grade 3–5 chemotherapy toxicity far better than performance status [8]. The CARG study did include 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%). Abnormal CA125 was associated with assistance with IADL, low PS, chemotherapy toxicity and dose reductions [13]. 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 older women with ovarian cancer. This includes low albumin (<35 g/L), low ADL score (<6), low IADL score (<25), lymphopenia (<1G/L) and a high Hospital Anxiety and Depression (HADS) score (>14) [14].

Chemotherapy

Background

Older women are less likely to be offered standard or for that matter, any chemotherapy. A Surveillance, Epidemiology and End Results Program (SEER)S-Medicare analysis showed that among women aged 65 years or older diagnosed with ovarian cancer between the years of 2001 and 2005, 29% received no chemotherapy, 25% received only a partial course of chemotherapy, and just 47% completed their planned chemotherapy course. Those aged older than 80 years were twice as likely to not complete chemotherapy, and those with two or more comorbidities were 83% more likely to not complete chemotherapy. The authors suggested that these results show that chemotherapy may be underused in elderly women [15], but high-level retrospective analyses cannot determine if the "underuse" of chemotherapy might, in fact, have been medically appropriate.

Older patients are more vulnerable to certain chemotherapy toxicities. The most common toxicities of platinum-taxane regimens, the usual first-line therapy for ovarian cancer, are cytopenias and neuropathy. This was highlighted in a large retrospective analysis of outcomes and toxicities seen in the 620 patients aged 70 years and older enrolled on Gynecologic Oncology Group (GOG) protocol 182, a phase III trial studying triplet-chemotherapy regimens for patients with newly diagnosed ovarian cancer [16]. Older women enrolled on such a trial are likely to be healthier than the average older woman with ovarian cancer, but older patients still had poorer performance status, lower completion rates of all 8 chemotherapy cycles and increased toxicities,

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