

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20242846>

Review Article

Strategies for managing epithelial ovarian cancer in elderly patients: a comprehensive review

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Received: 12 August 2024

Accepted: 06 September 2024

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ABSTRACT

The management of epithelial ovarian cancer in elderly patients presents distinct challenges due to age-related factors and comorbidities. Developing optimal strategies requires a careful balance between treatment efficacy and the potential side effects. This review aims to evaluate current management approaches specifically tailored to elderly patients with epithelial ovarian cancer. It focuses on the effectiveness and safety of various treatments, including surgery, chemotherapy, and targeted therapies, and considers how age-related factors influence treatment decisions and outcomes. Additionally, the review explores the importance of geriatric assessment and supportive care in optimizing treatment for this demographic. The findings suggest that managing epithelial ovarian cancer in elderly patients demands a multifaceted approach that considers both the effectiveness of the treatment and the patient's overall health and quality of life. By recognizing and addressing the unique needs of elderly patients, clinicians can refine treatment strategies, thereby improving outcomes for this vulnerable population. This approach emphasises the importance of individualized care that is responsive to the specific challenges posed by ageing and associated comorbidities, ultimately leading to better health outcomes for elderly patients with epithelial ovarian cancer.

Keywords: Elderly, Ovarian cancer, Older patients, Neoadjuvant chemotherapy

INTRODUCTION

Epithelial ovarian cancer represents a significant health concern, particularly among older women, with a median age at diagnosis of 63 years and 45.8% of cases occurring in individuals aged 65 years and older. In 2013 alone, there were an estimated 222,400 new cases diagnosed, resulting in 14,030 fatalities attributed to the disease.¹ Serous cancers, constituting 80%-85% of ovarian tumors, can manifest in various anatomical locations, including the ovaries, fallopian tubes, or primary peritoneum.² Regrettably, the majority of patients, approximately 70% present with advanced-stage disease, as there is a lack of an effective screening modality for early detection, thereby impeding efforts to enhance survival rates. Several factors contribute to the heightened risk of epithelial ovarian

cancer development, notably, those associated with uninterrupted ovulation, such as nulliparity or low parity. Additionally, a noteworthy familial predisposition exists, particularly in cases linked to breast-ovarian cancer syndrome (BRCA-1or-2) or hereditary non-polyposis colorectal cancer syndrome (HNPCC, Lynch II syndrome).

These genetic predispositions may lead to an earlier onset of the disease, with a mean age at diagnosis of 42.7 years, though occurrences can transpire across a broad age spectrum, including individuals over 70 years of age.^{3,4} Age, notably, emerges as a significant determinant in overall survival (OS) rates for epithelial ovarian cancer patients. However, the precise reasons underlying this correlation remain subject to investigation, with potential

factors encompassing delays in diagnosis, suboptimal treatment approaches, or inherent biological complexities.⁵⁻⁸ In addressing the multifaceted challenges posed by epithelial ovarian cancer, concerted efforts are warranted to advance both diagnostic strategies and therapeutic interventions, to optimize outcomes and mitigate the adverse impact of this formidable disease on affected individuals and communities alike. Elderly patients undergoing treatment for ovarian cancer often encounter unique challenges not typically present in their younger counterparts. These challenges encompass a spectrum of issues, including the burden of comorbidities, limitations in daily activities, cognitive decline, and geriatric syndromes.

Among these syndromes, polypharmacy assumes particular significance in the context of chemotherapy administration, given its potential implications for drug interactions and heightened toxicity risks, particularly concerning the cytochrome P450 system. Efforts are underway to formulate guidelines aimed at optimizing medication management to enhance treatment outcomes while minimizing adverse effects.^{9,10} Despite these complexities, studies consistently indicate that older patients can generally tolerate chemotherapy at doses comparable to younger cohorts, with minimal impact on quality of life (QOL).¹¹ Notably, it is physiological age rather than chronological age that emerges as a more reliable predictor of treatment-related toxicity. Functional capacity, which transcends conventional performance status metrics such as Karnofsky Performance Score (KPS) or Eastern Cooperative Oncology Group (ECOG) status, serves as a valuable determinant of both treatment tolerance and clinical outcomes, including survival and morbidity.

Optimal treatment planning and robust supportive care strategies are pivotal in maximizing therapeutic benefits for older patients. Interestingly, while clinical factors like age and disease stage, psychosocial elements such as familial support and access to transportation also significantly impact QOL outcomes. Consequently, ongoing research endeavours seek to quantify and compare QOL metrics among ovarian cancer patients, recognizing their profound implications for overall treatment efficacy.^{12,13} A notable subset analysis from the gynaecologic oncology group (GOG) 172 trial underscores the importance of personal well-being (PWB) in influencing treatment outcomes, including overall survival (OS).¹⁴

This finding underscores the imperative of holistic patient care approaches that encompass not only medical interventions but also address the psychosocial dimensions of the patient experience. This paper provides a comprehensive review of epithelial ovarian cancer treatment, with a specific focus on older patients. While much of the available data stems from subset analyses within larger studies, prospective research endeavours have been conducted and are currently ongoing. Notably,

the definition of "older" or "elderly" varies across studies, historically centred around 65 years due to medicare data but increasingly shifting towards a focus on patients over 70 years, given their heightened susceptibility to adverse events and vulnerability.

ROLE OF SURGERY IN ELDERLY PATIENTS

Retrospective data strongly supports the notion that optimal cytoreductive surgery (CRS) improves overall survival in advanced epithelial ovarian cancer (EOC), now defined as achieving less than 1 cm of residual disease or ideally, no visible residual disease. Recent prospective trials further confirm this survival benefit. However, controversy surrounds the role of neoadjuvant chemotherapy (NACT) followed by interval cytoreduction (iCRS) as a primary treatment strategy. While aggressive upfront surgery may lead to postoperative morbidity, NACT with iCRS is being considered for patients unable to tolerate extensive surgery. This shift reflects a move towards personalized treatment approaches based on individual patient factors, including comorbidities.¹⁵⁻¹⁷

Identified risk factors for postoperative morbidity after primary surgery for ovarian cancer include older age (over 75), poor performance status, low serum albumin, presence of ascites, and high preoperative CA 125 levels.¹⁸ Consequently, age plays a crucial role in determining the optimal initial therapy for advanced disease, especially regarding surgery and its timing.

The analysis conducted by Hightower et al from the American Cancer Society revealed a notable decrease in survival among patients over the age of 80 compared to their younger counterparts.¹⁹ This decline was attributed to a less aggressive surgical approach, with older women more inclined to undergo surgery performed by general surgeons rather than gynaecologic oncologists, resulting in suboptimal cytoreductive surgery. Furthermore, older patients were less likely to receive adjuvant chemotherapy, with only 42% undergoing such treatment compared to 69% of their younger counterparts. This finding regarding the reduced likelihood of older women undergoing aggressive surgical interventions has been corroborated by other studies.²⁰

Recent studies, predominantly from single tertiary institutions and reported by gynaecologic oncologists, have provided retrospective insights into the surgical outcomes for older women with ovarian cancer. While many suggest that older patients generally tolerate aggressive surgical approaches well, yielding similar overall survival rates to their younger counterparts, a subset of studies highlights significant morbidity among very elderly individuals, particularly those over 80. Notably, a study from Oklahoma observed a notable rate of mortality before hospital discharge and within 30 days post-surgery in women aged over 80 undergoing primary cytoreduction, despite achieving a 74% rate of optimal cytoreduction.²¹ Complications were prevalent, with 13%

unable to receive adjuvant chemotherapy, and only 57% completing more than three cycles of treatment. Population-based analyses further reinforce age as an independent risk factor for surgical morbidity. In the SEER analysis by Thrall et al., advancing age correlated significantly with a heightened 30-day mortality risk, with patients over 85 facing five times the mortality risk compared to those aged 65 to 69. Moreover, each year over 65 was associated with a 7.5% increase in mortality risk.²² Further risk modelling underscored that woman over 75, particularly those with stage IV disease or stage III disease with comorbidities, were at the highest risk of 30-day mortality following cytoreductive surgery. Consistently, data from the Nationwide Inpatient Sample registry also revealed an escalation of perioperative complications with advancing age.²³

Among 28,651 patients studied, complication rates increased with age, ranging from 17.1% in those under 50 to 29.7% in those aged 70-79 and 31.5% in those over 80. Similarly, discharge to a facility rose with age, from 1.0% in those under 50 to 14.0% in those aged 70-79 and 33.3% in those over 80. Multivariate analysis identified age, comorbidities, and radical procedures as key predictors of morbidity and mortality.²³ Wright et al analyzed SEER data for women aged 65 and older, finding that older age, comorbidities, mucinous tumors, and stage IV cancers correlated with lower rates of post-surgery chemotherapy and delayed initiation. These findings underscore the complexity of postoperative outcomes prediction, suggesting a need for nuanced patient selection for aggressive primary surgery versus alternative approaches like NACT and iCRS or primary chemotherapy alone.²⁴

Aletti et al's study highlighted the importance of considering tumor distribution, age, and nutritional status together to identify patients for whom aggressive upfront surgery may not improve overall survival.¹⁸ Prospective research is necessary to refine patient selection criteria for primary CRS, balancing potential benefits with risks, thereby optimizing outcomes in this vulnerable population.

OVARIAN CANCER CHEMOTHERAPY IN ELDERLY PATIENTS

Timing of chemotherapy: neoadjuvant chemotherapy

Neoadjuvant chemotherapy (NACT), administered before cytoreductive surgery (CRS), is increasingly utilized, particularly for older and frail patients. Reports suggest that NACT enhances the likelihood of achieving optimal CRS (defined as no residual disease post-surgery) with reduced surgical morbidity, without significantly impacting survival.²⁵ The sole prospective, randomized study comparing NACT to primary CRS followed by adjuvant chemotherapy is EORTC study 55971. This trial included 632 patients with stage IIIC or IV epithelial ovarian cancer (EOC), randomly assigned to either primary CRS followed by chemotherapy or NACT

followed by interval CRS and chemotherapy. Baseline characteristics were similar between groups, with median ages of 62 and 63, respectively, and no subgroup analysis based on older age was reported.²⁵ In the comparison between neoadjuvant chemotherapy (NACT) and primary debulking surgery, NACT showed non-inferiority with median overall survival times of 29 months and 30 months respectively. However, both arms exhibited relatively short median survival, suggesting the potential selection of patients with poor prognosis. The absence of gross residual disease emerged as a key predictor of survival, sparking ongoing controversy regarding the optimal approach for patients where achieving no residual disease is feasible.

The CHORUS trial, a phase III study with eligibility criteria mirroring EORTC 55971, showed no statistically significant difference in overall survival between primary debulking surgery (pCRS) and interval debulking surgery (iCRS) groups, with median survival times of 22.8 and 24.5 months, respectively.²⁶ Combining data from both trials yielded an overall hazard ratio of 0.93 (95% CI, 0.81 to 1.06), indicating comparable outcomes between the two approaches. Notably, patients in EORTC 55971 and CHORUS were approximately a decade older on average compared to previous GOG studies. A larger proportion exhibited poorer performance status (PS) and advanced-stage disease, indicating a highly selected, poor prognosis cohort.²⁷

In 2020, Fagotti et al reported comparable outcomes for patients with high tumour load assessed via laparoscopic examination. It's noteworthy that patients over 70 years old were excluded from the trial.²⁸ Older women, particularly those grappling with significant comorbidities and frailty, face heightened risks of surgical morbidity. In light of these considerations, neoadjuvant chemotherapy (NACT) emerges as a viable option for such individuals. While patient management necessitates individualized approaches, these criteria provide rational guidelines for considering NACT as a preferred strategy.

CHEMOTHERAPY AFTER PRIMARY SURGERY

Epithelial ovarian cancer (EOC) stands out as one of the most chemotherapy-sensitive diseases, exhibiting notably high initial response rates. The current standard of care has progressed towards taxane and platinum-based treatment regimens, with variations in scheduling and administration routes. However, it's crucial to note that the pivotal studies establishing these standards lacked representation from older patients, defined here as individuals aged 70 or above. The majority of participants in these trials were typically the most physically fit, with a high-performance status (PS). The pivotal trials such as GOG 158, which established paclitaxel and carboplatin as a standard regimen, and GOG 172, which established intraperitoneal cisplatin and paclitaxel-based therapy post optimal cytoreduction, included only a small fraction (12%) of patients aged over 70.^{16,29} Similarly, trials like GOG 218 and ICON 7, assessing the addition of bevacizumab to

paclitaxel and carboplatin every 21 days, enrolled 23% and 10% of patients aged over 70, respectively.^{30,31} Notably, GOG 182, one of the largest randomized trials in EOC with over 4,000 participants, comprised 23% of patients aged over 70.³²

Although specific subset analyses for the older population were not conducted in these trials, a post hoc analysis of GOG 182 revealed several notable findings among the 620 patients aged 70 or older. This cohort exhibited poorer performance status, lower completion rates of chemotherapy, increased incidences of toxicities (such as neuropathy and cytopenias), and an overall survival duration eight months shorter, even after adjusting for other prognostic factors.³³ The observed adverse outcomes among a highly selected cohort of older patients, who were considered sufficiently fit to participate in prospective clinical trials, underscore the challenge of evaluating treatment reserve in this demographic. Uncertainty regarding the tolerance levels of older individuals, compounded by concurrent comorbidities and social factors, likely contributes to the low utilization of standard-of-care chemotherapy for ovarian cancer in this population.

A SEER review examining chemotherapy use in advanced EOC revealed a decline in chemotherapy administration with increasing age. For instance, compared to the reference group aged 65 to 69, the odds ratios (ORs) for chemotherapy administration decreased to 0.65 for women aged 75 to 79, 0.24 for women aged 80 to 84, and 0.12 for women aged 85 and older.³⁴ Another SEER analysis identified women over 76 years old and those with two or more medical comorbidities as being at the highest risk of incomplete chemotherapy, with an OR of 1.64.³⁵ Clinical trials specifically designed for older and performance status-challenged women have been conducted primarily outside the United States. The inaugural trial dedicated to this demographic (GOG 273) was completed in the United States, providing valuable insights, albeit in abstract form in 2014, to guide optimal therapy selection for these patients.³⁶

CHEMOTHERAPEUTIC OPTIONS IN ELDERLY PATIENTS

Due to heightened concerns regarding excess toxicity in older women, research efforts have concentrated on enhancing tolerance without compromising effectiveness. These investigations primarily revolve around three key areas, initial dose adjustments, scheduling variations, and timing considerations, such as neoadjuvant versus primary chemotherapy.

INITIAL DOSE MODIFICATION

In 1997, the GINECO group in France initiated the Elderly Women Ovarian Cancer (EWOC) program, focusing on the specific needs of older patients. Over the period from 1998 to 2003, two prospective studies were conducted to

evaluate the tolerability of current standard platinum-based chemotherapy regimens in this population. Both studies enrolled women aged 70 or older, employing inclusive criteria and conducting baseline geriatric assessments (GA).

The initial study (EWOC 1) involved 83 patients (median age: 76) with stage III/IV EOC who received carboplatin (AUC 5) combined with cyclophosphamide (600 mg/m²) termed CC regimen and administered every 28 days for six cycles. Remarkably, 72% of patients completed all six cycles of the CC regimen with minimal toxicities.³⁷ Furthermore, GA emerged as a predictor of both toxicity and overall survival. Multivariate analysis identified three factors prognostic for toxicity: baseline depression symptoms ($p < 0.006$), dependence ($p < 0.048$), and a PS of 2 or greater ($p < 0.026$). Independent prognostic factors for overall survival, as per the Cox model, included depression ($p < 0.003$), International Federation of Gynaecology and Obstetrics (FIGO) stage IV ($p < 0.007$), and consumption of more than six medications per day ($p < 0.043$).

The subsequent study (EWOC 2) evaluated the feasibility of carboplatin (AUC 5) in combination with paclitaxel (175 mg/m²) - referred to as CP regimen - administered once every 3 weeks for six cycles in 75 older patients. The feasibility of completing all six cycles for patients receiving CP was noted at 68%.³⁸

A retrospective, multivariate analysis pooled data from two studies (EWOC 1 and EWOC 2) to examine predictive factors of survival. Notably, patients in EWOC 2 tended to be younger and had better performance status compared to those in EWOC 1, suggesting a potential selection bias driven by concerns about higher toxicity associated with the CP regimen. Indeed, the CP regimen exhibited more severe hematologic and neurologic toxicities compared to the CC regimen. Despite a higher proportion of patients with optimal cytoreductive surgery in the CP group, survival outcomes remained similar. Advanced age, baseline depression symptoms, and FIGO stage IV were identified as predictive factors for poor prognosis. Furthermore, the use of paclitaxel was independently associated with poorer survival.

However, due to the small, non-randomized nature of this study, the validity of these findings remains uncertain. GOG 273, currently underway, aims to provide further insights into this matter. This study enrolled women over 70 with newly diagnosed EOC, allowing treatment selection between combination therapy with paclitaxel and carboplatin plus peg filgrastim support or single-agent carboplatin. Although not randomized, both arms showed high completion rates of chemotherapy cycles, with overall improvements in quality of life, social activity, and daily function reported by patients. Additionally, the EWOC 3 study focused on evaluating single-agent carboplatin AUC 5 in a carefully selected, frail population. This study aimed to validate the geriatric vulnerability score (GVS) developed during the baseline geriatric

assessments conducted in EWOC 1 and 2, which will be further discussed in the subsequent section on geriatric assessments.³⁹

DOSAGE SCHEDULE IN ELDERLY PATIENT

The MITO-5 (Multicentre Italian trial in ovarian cancer) phase II study examined the tolerability of a weekly combination of carboplatin (AUC 2) and paclitaxel (60 mg/m²) administered on days 1, 8, and 15, every 4 weeks for six cycles. This trial included 26 patients aged 70 or older with stage IC to IV disease and performance status up to or less than PS 2. Notably, 54% of patients had at least two comorbidities and exhibited high functional dependency, with 31% reporting limitations in activities of daily living (ADL) and 69% in instrumental activities of daily living (IADL). The study reported a RECIST response rate of 38.5% and a median overall survival of 32.0 months. Toxicity remained low, with 89% of patients receiving treatment without any unacceptable defined toxicities, meeting the primary study endpoint.⁴⁰

The larger randomized phase III trial (MITO-7) compared the same weekly regimen utilized in MITO-5 against standard carboplatin (AUC 6) with paclitaxel (175 mg/m²) every 3 weeks in women newly diagnosed with EOC. While not specifically targeted at older women, this trial underscored the potential advantages of the weekly regimen. It demonstrated improved quality of life scores and reduced toxicity, notably lower rates of severe neuropathy and hematologic toxicity. Despite no survival advantage observed with the weekly regimen, there was no decrement either, with comparable median progression-free survival (17.3 vs 18.3 months). These findings suggest the weekly regimen is a viable alternative to the standard every-21-day paclitaxel and carboplatin, particularly beneficial for more vulnerable patient populations.⁴¹

In response to the interest sparked by recent phase III trials advocating for weekly dosing, the Gynaecologic Oncology Group (GOG) 273 trial introduced a weekly treatment arm, evaluating carboplatin AUC 5 alongside weekly paclitaxel at 60 mg/m². The primary aim of this arm is to assess whether an eight-point geriatric assessment (GA) score could effectively predict the tolerability of chemotherapy.

INTRAPERITONEAL CHEMOTHERAPY FOR OVARIAN CANCER

Cisplatin-based intraperitoneal chemotherapy offers significant survival benefits for patients with optimal cytoreductive surgery in stage III ovarian cancer, yet concerns persist regarding technical challenges and increased toxicities. In studies like GOG 172, older patients constituted a substantial portion of participants, but completion rates of the intraperitoneal regimen were low due to toxicity issues.

Applying these findings to older populations requires consideration of several factors. Firstly, intraperitoneal

cisplatin usage may pose challenges due to age-related declines in renal function, necessitating careful monitoring. Secondly, the use of paclitaxel warrants cautions due to age-related changes affecting drug clearance and heightened toxicities. Despite demonstrated survival advantages, widespread adoption of intraperitoneal therapy has been hindered by these limitations.

When considering intraperitoneal chemotherapy for older women, careful patient selection is crucial. This entails assessing functional status, kidney function, hearing ability, and recognizing the potential for earlier onset of toxicities compared to intravenous chemotherapy alone.^{42,43}

CHEMOTHERAPY FOR RECURRENT DISEASE

Treatment for recurrent ovarian cancer is stratified based on the timing of relapse following the last platinum-containing chemotherapy administration. Recurrence within 6 months, termed platinum-resistant, contrasts with relapse beyond 6 months, classified as platinum-sensitive. Clinical trials have underscored the survival benefit of combining carboplatin with either paclitaxel, liposomal doxorubicin, or gemcitabine for platinum-sensitive disease.^{44,45}

Notably, in the CALYPSO trial, the carboplatin-paclitaxel combination exhibited a higher incidence of neurologic toxicity, particularly neuropathy exceeding grade 2, among patients over 70 years old. While this demographic constituted only 16% of the study cohort, the lower incidence of severe neurologic toxicity supports pegylated liposomal doxorubicin over paclitaxel in older women.⁴⁶

Conversely, for platinum-resistant disease, single-agent chemotherapy is standard, yielding response rates ranging from 10% to 25% and a median duration of 4 to 8 months. Common options include liposomal doxorubicin, topotecan, gemcitabine, weekly paclitaxel, and single-agent bevacizumab.⁴⁷ Although data for older patients with ovarian cancer are limited, evidence from studies in lung and breast cancer suggests good tolerability of most single-agent drugs in this population. Gronlund et al, reported their findings on topotecan usage in 57 older patients with platinum-resistant ovarian cancer, observing comparable toxicity profiles and responses between older (≥ 65 years) and younger (< 65 years) cohorts. Performance status emerged as a superior predictor of response and survival in both groups.⁴⁸ Presently, liposomal doxorubicin or weekly topotecan are favoured among oncologists for older patients with platinum-resistant disease, given their improved toxicity profiles.⁴⁹

The recent AURELIA trial publication and the subsequent U.S. Food and drug administration (FDA) label approval for bevacizumab at 10 mg/kg every 2 weeks, in combination with pegylated liposomal doxorubicin (PLD) at 40 mg/m², weekly paclitaxel at 80 mg/m² for four doses,

or topotecan at 4 mg/m² weekly for three doses, have introduced yet another treatment option for the platinum-resistant population. The median age of patients receiving chemotherapy/bevacizumab was 62, ranging from 25 to 80 years.⁵⁰

Criticism of the study stemmed from the absence of a bevacizumab-alone arm, despite its recognized efficacy based on phase II data, lacking FDA approval for this specific indication. Concerns regarding hypertension and arterial thrombosis risk, particularly in older patients with more comorbidities, have been raised. However, recent data from a prospective phase III trial indicated a significantly reduced bowel perforation rate of 2.8% among patients treated with bevacizumab compared to 1.2% in those without, with age not identified as a risk factor for perforation.⁵¹

Given that these chemotherapy options primarily offer palliation, there is ongoing debate regarding the emphasis on improved supportive measures over additional chemotherapy. Notably, a study highlighted significant cost differences without appreciable survival improvement between ovarian cancer patients treated aggressively with chemotherapy versus those enrolled in hospice during their final months. Authors advocate for earlier hospice enrolment, particularly among older frail patients with poor prognoses.⁵²

ASSESSMENT OF OLDER WOMEN FOR CHEMOTHERAPY

Geriatric assessment (GA) serves as a comprehensive evaluation tool, offering insights into a patient's functional status, comorbidities, cognition, psychological well-being, social support, and nutritional status. In the context of cancer care, numerous studies have highlighted the predictive value of GA in assessing the risk of severe chemotherapy-related toxicity. However, a validated instrument tailored specifically for older patients with ovarian cancer is currently lacking. While various assessments are utilized in the older adult cancer population, further prospective studies are essential to enhance accuracy in determining a patient's suitability for surgery or chemotherapy.

PRE-SURGICAL ASSESSMENT

Traditional preoperative assessment models, such as the Lee, Eagle, and American society of anaesthesiologist's criteria, often overlook the multifaceted evaluation required for older patients. The preoperative assessment of cancer in the elderly (PACE) tool was developed to integrate elements of comprehensive geriatric assessment with surgical risk assessment tools, though gynaecologic patients were not initially included. While age showed no significant association with postoperative complications, 30-day morbidity was predicted by factors like instrumental activities of daily living (IADL), moderate to severe scores on the Brief Fatigue Inventory (BFI), and

abnormal performance status (PS). Extended hospital stays were foreseen by lower scores in basic activities of daily living (ADL), IADL, and poorer PS.^{53,54} In 2012, the American College of Surgeons released a position paper outlining optimal preoperative assessment practices for geriatric patients, employing a standard checklist.⁵⁵ Additionally, the timed up and go test has been identified as a predictor of 30-day surgical morbidity among patients aged 70 or older undergoing cancer surgery, particularly those involving laparotomy. This finding emerged from the PREOP study, which aimed to evaluate various presurgical assessments in older patients undergoing different cancer surgeries.⁵⁶

A unique multicentre study, NRG-CC002, is currently underway, exclusively focusing on women over 70 years old diagnosed with advanced ovarian or endometrial serous cancer. Before surgery or neoadjuvant chemotherapy (NACT), this study collects geriatric measures, including functional status, comorbidities, psychological well-being, social activity/support, nutrition, fatigue, and medication usage. These measures are utilized to calculate a risk score to predict major postoperative complications, aiding in informed decision-making regarding treatment approaches.

PRECHEMOTHERAPY ASSESSMENT

A concise screening test to evaluate toxicity risk in older vulnerable women with ovarian cancer undergoing chemotherapy is crucial. Examples include the vulnerable elders survey (VES-13) and the cancer and aging Research group (CARG)-GA and toxicity score. VES-13, a self-administered survey, assesses self-rated health, functional capacity, and physical performance. Meanwhile, CARG-GA, a feasible assessment, incorporates an 11-variable toxicity score, demonstrating superior prediction of severe chemotherapy toxicity compared to performance status.⁵⁷

The French GINECO group introduced the geriatric vulnerability score (GVS) based on trials in older women with ovarian cancer. GVS identifies high-risk factors such as low albumin, impaired daily activities, lymphopenia, and high anxiety and depression scores. Higher GVS correlates with worse overall survival, lower chemotherapy completion rates, increased severe adverse events, and more unplanned hospitalizations.³⁹ Validation studies with larger cohorts are ongoing, affirming the utility of GVS in identifying high-risk patients.

CONCLUSION

The evolving landscape of designated treatment trials for older and performance-challenged women with ovarian cancer is progressively refining our approach to treatment planning. The ongoing efforts to evaluate pretreatment assessments for older patients offer promising prospects for the development of objective, practical clinical tools. By reducing reliance on subjective decision-making and incorporating evidence-based practices, these initiatives

hold the potential to improve outcomes for all individuals affected by ovarian cancer. As we continue to advance our understanding and application of best practices, we move closer towards ensuring optimal care and better prospects for patients in this vulnerable population.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. National Cancer Institute. SEER Stat Fact Sheets: Ovary Cancer. Available at: <http://seer.cancer.gov>. Accessed on 2nd February 2014.
2. Soslow RA. Histologic subtypes of ovarian carcinoma: an overview. *Int J Gynecol Pathol.* 2008;27:161-74.
3. Chen S, Iversen ES, Friebel T, Finkelstein D, Weber BL, Eisen A, et al. Characterization of BRCA1 and BRCA2 mutations in a large United States sample. *J Clin Oncol.* 2006;24:863-71.
4. Tew WP, Lichtman SM. Ovarian cancer in older women. *Semin Oncol* 2008;35:582-9.
5. De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based study. *Lancet Oncol.* 2014;15:23-34.
6. Lichtman SM. How I treat ovarian cancer in older women. *J Geriatr Oncol* 2014;5:223-9.
7. Bouchardy C, Rapiti E, Blagojevic S, Vlastos AT, Vlastos G. Older female cancer patients: importance, causes, and consequences of undertreatment. *J Clin Oncol.* 2007;25:1858-69.
8. Fourcadier E, Trétarre B, Gras-Aygon C, Ecarnot F, Daurès JP, Bessaoud F. Under-treatment of elderly patients with ovarian cancer: a population based study. *BMC Cancer* 2015;15:937.
9. Nightingale G, Hajjar E, Swartz K, Andrel-Sendecki J, Chapman A. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and potentially inappropriate medication use among ambulatory senior adults with cancer. *J Clin Oncol.* 2015;33:1453-9.
10. Lichtman SM, Hollis D, Miller AA, Rosner GL, Rhoades CA, Lester EP, et al. Prospective evaluation of the relationship of patient age and paclitaxel clinical pharmacology: Cancer and Leukemia Group B (CALGB 9762). *J Clin Oncol.* 2006;24:1846-51.
11. Chen H, Cantor A, Meyer J, Beth Corcoran M, Grendys E, Cavanaugh D, et al. Can older cancer patients tolerate chemotherapy? A prospective pilot study. *Cancer.* 2003;97:1107-14.
12. Wenzel LB, Huang HQ, Armstrong DK, Walker JL, Cella D. Health-related quality of life during and after intraperitoneal versus intravenous chemotherapy for optimally debulked ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol.* 2007;25:437-43.
13. Vasey PA, Jayson GC, Gordon A, Gabra H, Coleman R, Atkinson R, et al. Phase III randomized trial of docetaxel-carboplatin versus paclitaxel-carboplatin as first-line chemotherapy for ovarian carcinoma. *J Natl Cancer Inst.* 2004;96:1682-91.
14. Von Gruenigen VE, Huang HQ, Gil KM, Frasure HE, Armstrong DK, Wenzel LB. The association between quality of life domains and overall survival in ovarian cancer patients during adjuvant chemotherapy: a Gynecologic Oncology Group Study. *Gynecol Oncol.* 2012;124:379-82.
15. Landrum LM, Java J, Mathews CA, et al. Prognostic factors for stage III epithelial ovarian cancer treated with intraperitoneal chemotherapy: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2013;130:12-18.
16. Ozols RF, Bundy BN, Greer BE. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2003;21(17):3194-200.
17. Hou JY, Kelly MG, Yu H. Neoadjuvant chemotherapy lessens surgical morbidity in advanced ovarian cancer and leads to improved survival in stage IV disease. *Gynecol Oncol.* 2007;105:211-7.
18. Aletti GD, Eisenhauer EL, Santillan A. Identification of patient groups at highest risk from traditional approach to ovarian cancer treatment. *Gynecol Oncol.* 2011;120:23-8.
19. Hightower RD, Nguyen HN, Averette HE. National survey of ovarian carcinoma. IV: patterns of care and related survival for older patients. *Cancer.* 1994;73:377-83.
20. Ries LA. Ovarian cancer. Survival and treatment differences by age. *Cancer.* 1993;71(2):524-9.
21. Moore KN, Reid MS, Fong DN. Ovarian cancer in the octogenarian: does the paradigm of aggressive cytoreductive surgery and chemo-therapy still apply? *Gynecol Oncol.* 2008;110:133-9.
22. Thrall MM, Goff BA, Symons RG. Thirty-day mortality after primary cytoreductive surgery for advanced ovarian cancer in the elderly. *Obstet Gynecol.* 2011;118:537-47.
23. Wright JD, Lewin SN, Deutsch I. Defining the limits of radical cytoreductive surgery for ovarian cancer. *Gynecol Oncol.* 2011;123:467-73.
24. Wright JD, Herzog TJ, Neugut AI. Effect of radical cytoreductive surgery on omission and delay of chemotherapy for advanced-stage ovarian cancer. *Obstet Gynecol.* 2012;120:871-81.
25. Vergote I, Trope CG, Amant F. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *New Engl J Med.* 2010;363:943-53.
26. Kehoe S, Hook J, Nankivel M. Chemotherapy or upfront surgery for newly diagnosed advanced ovarian cancer: results from the MRC CHORUS trial. *J Clin Oncol.* 2013;31:550.

27. Winter WE 3rd, Maxwell GL, Tian C. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2007;25:3621-7.
28. Fagotti A, Ferrandina MG, Vizzielli G. Randomized trial of primary debulking surgery versus neoadjuvant chemotherapy for advanced epithelial ovarian cancer (SCORPION- NCT01461850). *Int J Gynecol Cancer.* 2020;30:1657-64.
29. Armstrong DK, Bundy B, Wenzel L. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *New Engl J Med.* 2006;354:34-43.
30. Burger RA, Brady MF, Bookman MA. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *New Engl J Med.* 2011;365:2473-83.
31. Perren TJ, Swart AM, Pfisterer J. A phase 3 trial of bevacizumab in ovarian cancer. *New Engl J Med.* 2011;365:2484-96.
32. Bookman MA, Brady MF, McGuire WP. Evaluation of new platinum-based treatment regimens in advanced-stage ovarian cancer: a phase III trial of the Gynecologic Cancer Intergroup. *J Clin Oncol.* 2009;27:1419-25.
33. Tew WP. Treatment outcomes for older women with advanced ovarian cancer: results from a phase III clinical trial (GOG 182). *J Clin Oncol.* 2010;28:15.
34. Sundararajan V, Hershman D, Grann VR. Variations in the use of chemotherapy for elderly patients with advanced ovarian cancer: a population-based study. *J Clin Oncol.* 2002;20:173-8.
35. Fairfield KM, Murray K, Lucas FL. Completion of adjuvant chemotherapy and use of health services for older women with epithelial ovarian cancer. *J Clin Oncol.* 2011;29:3921-6.
36. Von Gruenigen VE, Huang H, Tew WP. Geriatric assessment and tolerance to chemotherapy in elderly women with ovarian, primary peritoneal or fallopian tube cancer: a Gynecology Oncology Group study. *Gynecol Oncol.* 2014;133:439.
37. Freyer G, Geay JF, Touzet S. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. *Ann Oncol.* 2005;16:1795-1800.
38. Tre'dan O, Geay JF, Touzet S. Carboplatin/cyclophosphamide or carboplatin/paclitaxel in elderly patients with advanced ovarian cancer? Analysis of two consecutive trials from the Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens. *Ann Oncol.* 2007;18:256-62.
39. Falandry C, Weber B, Savoye AM. Development of a geriatric vulnerability score in elderly patients with advanced ovarian cancer treated with first-line carboplatin: a GINECO prospective trial. *Ann Oncol.* 2013;24:2808-13.
40. Pignata S, Breda E, Scambia G. A phase II study of weekly carboplatin and paclitaxel as first-line treatment of elderly patients with advanced ovarian cancer. A multicentre Italian trial in ovarian cancer (MITO-5) study. *Crit Rev Oncol Hematol.* 2008;66:229-36.
41. Pignata S, Scambia G, Katsaros D. Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncol.* 2014;15:396-405.
42. Lichtman SM, Wildiers H, Launay-Vacher V. International Society of Geriatric Oncology (SIOG) recommendations for the adjustment of dosing in elderly cancer patients with renal insufficiency. *Eur J Cancer.* 2007;43:14-34.
43. Lichtman SM, Hollis D, Miller AA. Prospective evaluation of the relationship of patient age and paclitaxel clinical pharmacology: Cancer and Leukemia Group B (CALGB 9762). *J Clin Oncol.* 2006;24:1846-51.
44. Parmar MK, Ledermann JA, Colombo N. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. *Lancet.* 2003;361:2099-106.
45. Pfisterer J, Plante M, Vergote I. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol.* 2006;24:4699-707.
46. Kurtz JE, Kaminsky MC, Floquet A. Ovarian cancer in elderly patients: carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in late relapse-a Gynaecologic Cancer Intergroup (GCIg) CALYPSO sub-study. *Ann Oncol.* 2011;22:2417-23.
47. Bukowski RM, Ozols RF, Markman M. The management of recurrent ovarian cancer. *Semin Oncol.* 2007;34(2):1-15.
48. Gronlund B, Høgdall C, Hansen HH. Performance status rather than age is the key prognostic factor in second-line treatment of elderly patients with epithelial ovarian carcinoma. *Cancer.* 2002;94:1961-7.
49. Gordon AN, Tonda M, Sun S. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. *Gynecol Oncol.* 2004;95:1-8.
50. Pujade-Lauraine E, Hilpert F, Weber B. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial. *J Clin Oncol.* 2014;32:1302-8.
51. Burger RA, Sill MW, Monk BJ. Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2007;25:5165-71.

52. Lewin SN, Buttin BM, Powell MA. Resource utilization for ovarian cancer patients at the end of life: how much is too much? *Gynecol Oncol.* 2005;99:261-6.
53. Audisio RA, Pope D. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. *Crit Rev Oncol Hematol.* 2008;65:156-63.
54. Pope D, Ramesh H, Gennari R. Pre-operative assessment of cancer in the elderly (PACE): a comprehensive assessment of underlying characteristics of elderly cancer patients prior to elective surgery. *Surg Oncol.* 2006;15:189-97.
55. Chow WB, Rosenthal RA, Merkow RP. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg.* 2012;215:453-66.
56. Huisman MG, van Leeuwen BL, Ugolini G. Timed up and go: a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A multicentre cohort study. *PloS One.* 2014;9:86863.
57. Won E, Hurria A, Feng T. CA125 level association with chemotherapy toxicity and functional status in older women with ovarian cancer. *Int J Gynecol Cancer.* 2013;23:1022-8.

Cite this article as: Gupta S, Kalwaniya DS. Strategies for managing epithelial ovarian cancer in elderly patients: a comprehensive review. *Int J Reprod Contracept Obstet Gynecol* 2024;13:2974-82.