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Clinicopathologic Features and Survival Outcomes in Women Aged 80 Years or Older with Advanced Ovarian Cancer

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ABSTRACT

Objective: Women aged ≥80 years with ovarian cancer (OC) are significantly underrepresented in clinical trials, and their optimal management remains poorly defined. This study aimed to evaluate clinicopathologic characteristics and survival outcomes in this understudied population.

Material and Methods: This retrospective study included 43 women aged ≥80 years diagnosed with advanced OC between 2009 and 2024 at a tertiary care center. Clinical, pathological, and treatment data were collected. Kaplan-Meier and Cox regression analyses were used to evaluate time to progression (TTP) and overall survival (OS).

Results: The mean age was 83.4±4.1 years (range: 80-101); 95.3% had at least one comorbidity, and 46.5% had polypharmacy. Despite advanced age, 86% of patients underwent cytoreductive surgery and 79.1% received chemotherapy. Optimal cytoreduction (≤1 cm) was achieved in 89.2% of surgically treated patients, with no gross residual disease (R0) obtained in 64.9%. During a median follow-up period of 21.4 months, 76.7% of patients died. The median TTP was 20.9 months [95% confidence interval (CI): 0.0-42.8], and the median OS was 27.1 months (95% CI: 14.9-39.2). The 2 years TTP and OS rates were 49.4%±9.3 and 56.2%±7.8, respectively. Notably, cytoreductive surgery was associated with improved OS (hazard ratio: 0.171; p=0.001).

Conclusion: Cytoreductive surgery can achieve high rates of optimal and complete resection in carefully selected women aged ≥80 years with advanced OC when performed at experienced, high-volume centers. These findings indicate that advanced chronological age alone should not be considered a contraindication to surgical evaluation in fit octogenarians.

Keywords: Ovarian cancer; elderly; cytoreductive surgery; polypharmacy

INTRODUCTION

Ovarian cancer (OC) is a major global health concern and remains one of the most lethal gynecologic malignancies.[1] The disease disproportionately affects older women, with the incidence increasing with age and peaking in the seventh decade of life.[2] Nearly half of all OC cases occur in women over 65, who also account for more than 70% of disease-related deaths.[3] As global life expectancy rises, the number of elderly women diagnosed with OC is expected to increase, presenting a growing clinical challenge for gynecologic oncologists.[4]

Despite this high disease burden, older patients are often undertreated. They are less likely than younger patients to undergo optimal cytoreductive surgery or to receive standard chemotherapy.[3,5] This trend is frequently attributed to concerns regarding comorbidities, functional limitations, and a higher perceived risk of treatment-related complications.[6,7] Compounding this issue is the historical underrepresentation of elderly women in clinical trials that inform standard-of-care guidelines, leading to limited evidence-based strategies tailored to this population.[4,8]

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Notably, women aged 80 years and older remain especially underrepresented in the literature, and their clinical characteristics and outcomes are poorly understood.[9] The primary objective of this study was to evaluate the clinicopathologic features and survival outcomes in a cohort of Turkish women aged 80 years or older diagnosed with advanced OC. By providing real-world data on this distinct and understudied group, the study aims to inform more appropriate management strategies and contribute to the limited body of evidence in this field.

MATERIAL AND METHODS

Study Design and Patient Selection

This retrospective cohort study included women aged ≥80 years who were newly diagnosed, treatment-naïve, and had advanced [defined as International Federation of Gynecology and Obstetrics (FIGO) stage III or IV] OC, followed at our tertiary care center between July 2009 and December 2024. A total of 917 patients with OC were initially screened. Patients younger than 80 years, those with early-stage disease, or those with duplicate records, those with missing key clinical or pathological data, those lost to follow-up, those who received initial treatment at an external institution, or those with synchronous malignancies were excluded. Therefore, the final cohort consisted of patients with complete data for all analyzed variables. Treatment strategies, including the decision to proceed with cytoreductive surgery, were individualized. Surgical selection required that the patient have an acceptable clinical performance status (typically independent in activities of daily living), no severe uncompensated comorbidities (such as advanced organ failure), and a manageable estimated tumor burden. Final surgical decisions were based on multidisciplinary team tumor board consensus and pre-anesthesia evaluations. After these criteria were applied, 43 women constituted the final study cohort. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Başkent University Rectorate Medical and Health Sciences Research Board (approval number: KA25/254, date: 25.06.2025). Because the study was retrospective, the requirement for informed consent was waived.

Data Collection

All data were retrieved from the institutional electronic medical records. Variables collected included demographic and clinical information (age at diagnosis, presence and number of comorbidities, and number of regularly used medications). Additionally, baseline laboratory values, including serum albumin and total lymphocyte count, were collected to calculate the prognostic nutritional index (PNI), a surrogate marker of nutritional and immunological status, with higher values indicating greater nutritional reserve and reduced frailty. PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3) and dichotomized based on the median value. Pathologic features included histological subtype and tumor grade. In patients who underwent cytoreductive surgery [either primary debulking surgery (PDS), or interval debulking surgery (IDS)], additional data were collected on ovarian capsule rupture, lymphovascular invasion (LVI), lymph node involvement, and the surgical stage according to the 2014 FIGO classification. Data on systemic therapies across treatment lines were also collected.

Outcomes

The primary objective was to assess the clinicopathologic characteristics and survival outcomes among elderly women with OC. Polypharmacy was defined as the concurrent use of five or more medications. Time to progression (TTP) was defined as the interval between surgery and either radiological or clinical evidence of disease progression. TTP was chosen over standard progression-free survival to avoid counting non-cancer-related deaths in this elderly cohort as progression events. Because TTP was used to assess the durability of surgical cytoreduction, patients managed non-surgically were excluded from this analysis. Overall survival (OS), conversely, was calculated for the entire cohort and defined as the time from initial diagnosis to death from any cause or until last follow-up for censored cases.

Statistical Analysis

Statistical analyses were performed using IBM® SPSS Statistics, version 25. Baseline characteristics were summarized using descriptive statistics. Kaplan-Meier analysis was used to estimate survival curves, with group comparisons performed using the log-rank test. Univariable Cox proportional hazards regression was used to identify variables associated with TTP and OS. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported, and two-sided p-values <0.05 were considered statistically significant.

RESULTS

A total of 43 women with a mean age of 83.4±4.1 years (range: 80-101) were included in the study. The majority of patients (95.3%) had at least one comorbid condition, and polypharmacy (≥5 medications) was observed in 46.5% of cases. The median baseline PNI of the cohort was 41.0 (range: 21.9-57.5). Despite advanced age and comorbidities, the rate of cytoreductive surgery was 86.0%. PDS was performed in 33 patients, while IDS was conducted in 4 patients. Thirteen patients (35.1%) underwent extended surgery, which

included standard cytoreduction plus major upper abdominal procedures such as splenectomy (n=7) and bowel resection (n=6). Optimal cytoreduction (≤1 cm residual disease) was achieved in 33 patients (89.2%), while no gross residual disease (R0) was obtained in 24 patients (64.9%). Stoma formation was required in 3 patients (8.1%). Additionally, 2 patients (4.7%) underwent secondary cytoreductive surgery after the first progression. The 30 days postoperative mortality rate among surgically treated patients was 8.1% (3/37). Baseline clinical and pathological characteristics are summarized in Table 1.

A total of 34 patients (79.1%) received at least one cycle of chemotherapy, with a median of 1 treatment line (range: 1-4). The most commonly administered first-line regimen was paclitaxel plus carboplatin (31/34, 91.2%); subsequent-line regimens varied. Based on their clinical response following completion of initial first-line platinum-based therapy, 31 (93.9%) patients were classified as platinum-sensitive, and 2 (6.1%) were classified as platinum-resistant after developing disease progression within 6 months. Second-line, third-line, and fourth-line treatment rates were 34.9% (n=15), 11.6% (n=5), and 4.7% (n=2), respectively.

During a median follow-up of 21.4 months (range: 0.4-132.7), 33 patients (76.7%) died. The median TTP was 20.9 months (95% CI: 0.0-42.8), while the median OS was 27.1 months (95% CI: 14.9-39.2). The 2 years TTP and OS rates were 49.4%±9.3 and 56.2%±7.8, respectively (Figure 1). In univariable analyses, age ≥85 years (vs. 80-84 years), ≥3 comorbid conditions, polypharmacy, PNI (<41 vs. ≥41), high-grade serous histology, LVI, para-aortic lymph node involvement, or FIGO stage IV disease (vs. III) were not significantly associated with TTP (Table 2). OS outcomes were generally consistent with TTP findings. Notably, the receipt of cytoreductive surgery was significantly associated with improved OS (HR: 0.171; 95% CI: 0.061-0.477; p=0.001) (Figure 2).

DISCUSSION

This study provides real-world data on the clinicopathologic features and survival outcomes of women aged 80 years or older with advanced OC, who remain significantly underrepresented in clinical research.[10,11] Our findings demonstrate that in a carefully selected cohort, aggressive treatment is feasible and associated with meaningful outcomes. The median OS was 27.1 months, and univariable analysis showed that cytoreductive surgery was significantly associated with improved survival. These results challenge the common practice of undertreating the oldest old based solely on chronological age and highlight the importance of assessing physiological rather than chronological age.

TABLE 1: Baseline characteristics.

Characteristics	Total 43 patients
Age at diagnosis, mean ± SD, years	83.4±4.1
Age categories, n (%)	
80-84 years	29 (67.4)
85-89 years	11 (25.6)
≥90 years	3 (7.0)
Presence of comorbid disease(s), n (%)	41 (95.3)
Comorbidities, n (%)	
Hypertension	37 (86.0)
Coronary artery disease	19 (44.2)
Diabetes mellitus	17 (39.5)
Malignancy	5 (11.6)
Chronic kidney disease	4 (9.3)
Heart failure	2 (4.7)
Number of comorbidities, median (range)	2 (0-5)
Number of drugs used, median (range)	4 (0-11)
Polypharmacy (≥5 drugs), n (%)	20 (46.5)
PNI, median (range)	41.0 (21.9-57.5)
Histological subtype, n (%)	
High-grade serous	39 (90.7)
Low-grade serous	2 (4.7)
Non-serous	2 (4.7)
Cytoreductive surgery, n (%)	37 (86.0)
Primary debulking surgery	33/37 (89.2)
Interval debulking surgery	4/37 (10.8)
Extended surgery[&], n (%)	13/37 (35.1)
Optimal cytoreduction (≤1 cm), n (%)	33/37 (89.2)
No gross residual disease (R0), n (%)	24/37 (64.9)
Secondary cytoreductive surgery, n (%)	2 (4.7)
Stoma formation, n (%)	3 (8.1)
Ruptured ovarian capsule*, n (%)	35/37 (94.6)
Lymphovascular invasion*, n (%)	29/37 (78.4)
Lymph node involvement*, n (%)	
Pelvic	11/37 (29.7)
Paraaortic	2/37 (5.4)
Both	8/37 (21.6)
FIGO surgical staging*, n (%)	
III	32/37 (86.5)
IV	5/37 (13.5)

[&] Standard cytoreduction plus major upper abdominal organ resection.
* For patients who underwent debulking surgery.
FIGO: International Federation of Gynecology and Obstetrics; PNI: Prognostic nutritional index; SD: Standard deviation.

TABLE 2: Univariate Cox regression analyses for time to progression and overall survival.

Parameters	Time to progression (events=16)			Overall survival (events=33)		
	HR	95% CI	p-value	HR	95% CI	p-value
Age ≥85 years (vs. 80-84 years)	1.894	0.685-5.236	0.219	1.443	0.694-2.999	0.326
≥3 Comorbidities	1.365	0.495-3.765	0.548	1.766	0.874-3.566	0.113
Polypharmacy (≥5 drugs)	1.128	0.409-3.116	0.816	1.796	0.890-3.621	0.102
PNI ≥41 (vs. <41)	0.628	0.234-1.685	0.355	0.905	0.441-1.855	0.785
High-grade serous histology	1.127	0.254-5.005	0.876	1.164	0.397-3.411	0.782
Cytoreductive surgery	-	-	-	0.171	0.061-0.477	0.001
Lymphovascular invasion	2.907	0.657-12.86	0.159	1.122	0.443-2.843	0.808
Paraaortic LN involvement	0.307	0.069-1.372	0.122	0.826	0.342-1.996	0.672
FIGO stage IV (vs. III)	2.779	0.787-9.814	0.112	1.059	0.352-3.183	0.919

* Bold text indicates statistical significance at p<0.05 level.
CI: Confidence interval; FIGO: International Federation of Gynecology and Obstetrics; HR: Hazard ratio; LN: Lymph node; PNI: Prognostic nutritional index.

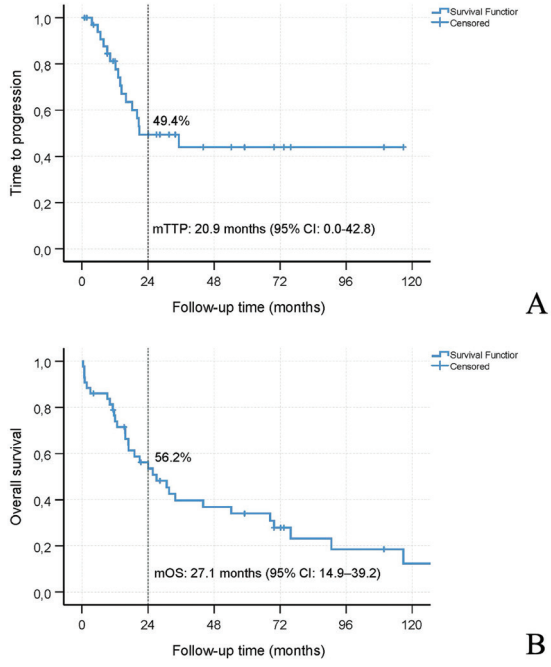

FIGURE 1: Kaplan-Meier curves for time to progression (A) and overall survival (B).

OS: Overall survival; CI: Confidence interval; TTP: Time to progression

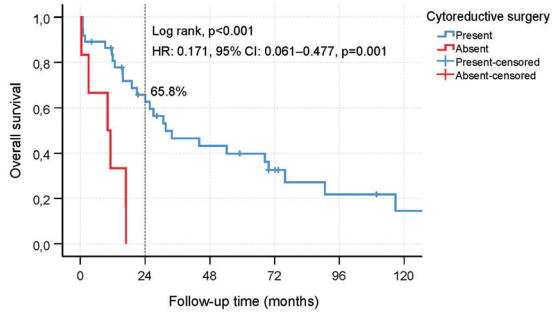

FIGURE 2: Kaplan-Meier curve for overall survival stratified by cytoreductive surgery.

HR: Hazard ratio; CI: Confidence interval

A key finding is the significant survival benefit conferred by cytoreductive surgery (HR: 0.171; p=0.001). In our cohort, a notably high proportion (86%) underwent surgery, likely contributing to the favorable median OS. This contrasts sharply with population-based studies in which elderly patients are frequently denied surgery. For instance, a recent registry study reported that only 27% of women aged ≥80 received both surgery and chemotherapy,[11] while other reports consistently show lower rates of guideline-concordant care in older adults.[12,13] Our results align with evidence from specialized centers demonstrating that selected elderly (≥65) and very elderly (≥75) patients can tolerate radical procedures and achieve cytoreduction rates comparable to younger cohorts.[14-16] These findings reinforce that maximal cytoreduction remains a cornerstone of OC management, even in the oldest old.[17,18]

In our cohort, 89.2% of surgically treated patients achieved optimal cytoreduction (≤1 cm residual disease), with 64.9% having no gross residual disease (R0), rates that compare favorably with those reported in large multicenter analyses. For instance, a combined exploratory analysis of three randomized trials by du Bois et al.[19] demonstrated that only 33.5% of patients achieved complete resection (R0), while 31.2% had small residual tumor burden (1-10 mm), and 35.3% had macroscopic residual disease exceeding 1 cm. Notably, their multivariate analysis showed that complete resection was associated with the most significant improvement in progression-free survival and OS compared with patients who had any residual disease, underscoring the critical prognostic impact of complete cytoreduction. Similarly, Bristow et al.[20], in a meta-analysis evaluating 81 cohorts encompassing 6,885 patients with stage III-IV ovarian carcinoma, reported that each 10% increase in maximal cytoreduction rate was associated with a 5.5% increase in median survival time. Cohorts achieving ≤25% maximal cytoreduction had a median survival of 22.7 months, whereas those with >75% maximal cytoreduction had a median survival of 33.9 months,

representing a 50% improvement. Our cohort's optimal cytoreduction rate, exceeding 75%, likely contributed to the relatively favorable median OS of 27.1 months despite the advanced age and comorbidity burden of the population.

Additionally, Eisenhauer et al.[21] reported that patients who required extensive upper abdominal procedures to achieve optimal cytoreduction had a median OS that was not reached at 68 months, compared to 84 months for those optimally cytoreduced with standard techniques and only 38 months for patients who were suboptimally cytoreduced. While our study did not include a formal comparison based on the extent of upper abdominal surgery, 35.1% of our patients underwent extensive surgical procedures, including splenectomy and bowel resection, supporting the feasibility of aggressive surgery in selected octogenarians. Importantly, their findings highlighted that patients requiring extensive procedures to achieve optimal cytoreduction had survival outcomes comparable to those optimally cytoreduced by standard surgery, reinforcing that tumor biology, rather than resection extent per se, drives prognosis.

Furthermore, Aletti et al.[22] demonstrated that residual disease was the strongest independent predictor of survival in patients with stage IIIC OC, and minimizing residual disease through aggressive surgical resection was beneficial, especially in those with carcinomatosis. In their study, the use of radical procedures to achieve optimal cytoreduction was associated with a significant survival advantage, increasing five-year disease-specific survival from 17% to 44% among patients with peritoneal carcinomatosis. Taken together, these studies corroborate our findings that achieving optimal cytoreduction, particularly R0 resection, is critical for improving survival even in the oldest-old. Our cohort's high rates of optimal and complete cytoreduction are notable, likely reflecting surgical expertise at our tertiary center; optimal resection rates vary significantly between institutions and often exceed 75% only at specialized centers.[20]

Interestingly, in univariable analyses, none of the traditional risk factors including age ≥85 years, number of comorbidities, high-grade serous histology, LVI, para-aortic lymph node involvement, or stage IV disease were significantly associated with TTP or OS. The prognostic impact of frailty, which encompasses factors beyond comorbidities, such as functional status, nutrition, and cognition, is increasingly recognized as more critical than age itself.[23,24] Validated tools, such as the geriatric vulnerability score, have been shown to have high prognostic performance for survival, superior to that of age.[25] Similarly, markers of nutritional status and sarcopenia are strongly associated with outcomes in OC patients.[26,27] Although polypharmacy did not reach statistical significance as a predictor in our study, it remains an important clinical marker warranting further evaluation in larger cohorts.[14]

The survival outcomes in our cohort are noteworthy. The median OS of 27.1 months for women aged ≥80 is comparable to outcomes reported for younger "elderly" cohorts. For example, Liontos et al.[23] reported a median OS of 30.2 months for patients older than 70 years, while Ferrero et al.[24] observed a median survival of 30 months in patients older than 75. Importantly, all our patients had advanced-stage disease, yet their survival was comparable to that of younger elderly cohorts with a broader distribution of disease stages. The encouraging survival observed in our much older advanced-stage cohort likely reflects the high rates of standard treatment, including both surgery and platinum-based chemotherapy. This suggests that when treatment is not withheld because of age, women in their ninth decade of life and beyond can achieve outcomes similar to those of their younger counterparts. Furthermore, studies that have controlled for selection bias have shown that neoadjuvant chemotherapy and PDS yield similar survival in elderly women, particularly those over 80 or with stage IV disease, supporting the use of tailored surgical strategies in this population.[28,29]

Study Limitations

This study has several limitations inherent in its design. Being a retrospective, single-center analysis, it is susceptible to selection bias. Patients treated at an experienced tertiary care center may be more motivated than the general population, which could explain the high rates of surgery and the favorable outcomes observed. The small sample size severely limited the statistical power of our analyses. Consequently, the lack of statistical significance for well-established prognostic factors, such as FIGO stage, LVI, and tumor histology, must be strictly interpreted as a type II error due to insufficient statistical power, rather than as a true absence of biological effect in this age group. Furthermore, since only cytoreductive surgery emerged as a significant predictor in the univariable analysis and the number of events was limited, a formal multivariable Cox regression was not performed to avoid statistical overfitting. Without multivariable adjustment, our finding that surgery improves survival is not definitive and must be interpreted strictly as hypothesis-generating. While representing a limitation to statistical power, the small sample size also reflects a broader clinical reality: even in high-volume centers like ours, the number of patients over 80 receiving treatment is very low. This is often due to a prevailing tendency to avoid aggressive therapies in this age group. A major limitation of our study is that it does not define the specific criteria for selecting patients for surgery. Although our results show that cytoreductive surgery provides a significant survival benefit, they do not identify which patients are ideal candidates or what the optimal selection criteria should be. This limitation primarily

stems from the retrospective nature of our analysis. While our surgical team undoubtedly performed thorough preoperative assessments, specific details such as functional status and comprehensive laboratory data were not systematically recorded, preventing a rigorous and standardized evaluation. The absence of formal geriatric assessment data is another major shortcoming; polypharmacy and PNI were used as proxies, but they cannot replace a comprehensive evaluation of frailty. Calculating TTP from the date of surgery introduces a non-uniform starting point between patients undergoing PDS and the small subset of patients (n=4) undergoing IDS because the duration of neoadjuvant chemotherapy is excluded from the time-to-event calculation. While the very low number of interval debulking cases likely minimizes the impact of this lead-time bias on the overall cohort estimates, it remains a methodological limitation. Despite these limitations, our study delivers a crucial message: successful cytoreductive surgery with high rates of optimal and R0 resection is achievable in patients aged 80 and over and is associated with improved OS in this selected cohort. The primary conclusion is that advanced age and the presence of large-volume disease at diagnosis should not be regarded as absolute contraindications to potentially curative-intent surgery. Instead, these patients warrant careful multidisciplinary evaluation. The critical next step for the field is to move beyond simply showing that surgery is possible and to focus on determining for whom it is appropriate. Larger-scale prospective studies are urgently needed to establish robust, evidence-based selection criteria that incorporate comprehensive geriatric assessments to ensure that appropriate patients receive appropriate treatment.

CONCLUSION

Our study demonstrates that selected women aged 80 years and older with advanced OC can tolerate standard treatment, which is associated with clinically meaningful survival outcomes. Chronological age alone should not be considered an absolute contraindication to curative-intent therapy. Instead, treatment decisions should be individualized on the basis of a comprehensive assessment of each patient's physiological status, functional reserve, and overall fitness. Importantly, the high rates of surgery and favorable survival outcomes observed in this study reflect a carefully selected cohort of octogenarians treated at an experienced tertiary center. Accordingly, aggressive treatment strategies should be reserved for patients who are rigorously evaluated and managed in high-volume centers with multidisciplinary expertise. With meticulous preoperative assessment and optimal surgical management, selected women aged 80 years and older can achieve high rates of complete cytoreduction and survival outcomes that approach those reported in younger elderly cohorts.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Başkent University Rectorate Medical and Health Sciences Research Board (approval number: KA25/254, date: 25.06.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.I., H.A., A.F., Ö.A., N.Ö., Ü.E.K., Concept: R.I., H.A., Ö.A., N.Ö., Ü.E.K., Design: R.I., H.A., Ö.A., N.Ö., Ü.E.K., Data Collection or Processing: R.I., H.A., A.F., Analysis or Interpretation: R.I., H.A., Ö.A., N.Ö., Ü.E.K., Literature Search: R.I., H.A., Writing: R.I., H.A.

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