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Factors associated with declining cytoreductive surgery in advanced epithelial ovarian cancer: a population-based study

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Abstract

Objective Cytoreductive surgery serves as a cornerstone intervention for advanced epithelial ovarian cancer (EOC), yet some patients decline the procedure despite clinical recommendations. This study aimed to evaluate survival outcomes and identify sociodemographic and clinical factors associated with this decision in advanced EOC patients.

Methods A retrospective analysis of EOC cases from the Surveillance, Epidemiology, and End Results (SEER) database (2004–2021) was conducted, including patients with stage III/IV EOC recommended for surgery. Patients were categorized into surgical and non-surgical cohorts. Propensity Score Matching (PSM) was applied to adjust for baseline differences, and survival outcomes were compared using Kaplan-Meier and Cox proportional hazards models. Logistic regression analysis was performed to identify predictors of surgery declination.

Results Of the 21,988 patients included, 363 (1.7%) were in the non-surgery group. Following a median follow-up of 33 months, patients in the non-surgical cohort demonstrated significantly lower overall survival (OS) compared to the surgical cohort, with mean OS of 17.8 months versus 45.8 months, respectively ($P < 0.001$). The Cox model showed increased mortality risk for the non-surgical group post-PSM (HR, 1.87; 95% CI, 1.62–2.15). Non-Hispanic Black, older age, lower household income, nonmetropolitan residence, and unmarried status were associated with higher odds of surgery refusal.

Conclusion Declining surgery is associated with significantly poorer survival in advanced EOC. Sociodemographic factors play a key role in surgical decision-making, underscoring the need for targeted interventions to improve access to surgical care and reduce disparities in EOC treatment outcomes. Further studies should explore the impact of specific chemotherapy and comorbidities on surgery refusal and survival.

Keywords Epithelial ovarian cancer, Surgery refusal, Sociodemographic disparities, SEER

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Introduction

Epithelial ovarian cancer (EOC) is the second most prevalent gynecologic malignancy and remains a leading cause of cancer-related death among women globally [1, 2]. The lack of effective screening modalities, coupled with nonspecific and often late-onset symptoms, results in most EOC cases being identified at advanced stages [3]. This delayed diagnosis is associated with a poor prognosis, with a 5-year survival rate for advanced-stage disease estimated at approximately 30% [4].

Cytoreductive (debulking) surgery remains the cornerstone of initial management for patients with advanced EOC [5, 6]. This procedure aims for maximal reduction of tumor burden, often necessitating a total abdominal hysterectomy, bilateral salpingo-oophorectomy (removal of ovaries and fallopian tubes), omentectomy (removal of the omentum), and resection of all macroscopically visible tumors [7]. Achieving optimal cytoreduction—defined as complete resection of visible tumors or reducing residual disease to less than 1 cm—has been shown to be a crucial predictor of improved survival outcomes [8, 9]. Nevertheless, a subset of patients recommended for surgery ultimately does not undergo the procedure [10].

The reasons for surgery refusal are varied. Socioeconomic factors, such as lower income and limited healthcare access, can prevent patients from getting surgery. Frailty and comorbidities, like heart disease or diabetes, may also make surgery seem too risky. Additionally, physician biases, such as those based on age or race, could influence whether surgery is recommended. These factors, together with medical, psychological, and social influences, affect patients' decisions to decline surgery. Analyzing the clinical outcomes in this population offers essential insights into treatment disparities.

This study assessed the clinical outcomes of patients with advanced EOC who were recommended for surgery yet did not undergo the procedure, using data from the Surveillance, Epidemiology, and End Results (SEER) database. In addition, the study evaluated sociodemographic and clinicopathologic characteristics associated with the decision to decline surgery. The insights gained from this analysis aim to guide initiatives that promote acceptance of surgical treatment and support the pursuit of equitable health outcomes for individuals diagnosed with advanced EOC.

Methods

Study design and data sources

This study employed a retrospective analysis of data from the SEER 17 database to investigate adult patients diagnosed with advanced EOC from 2004 to 2021. Representing approximately 26.5% of the U.S. population, the SEER 17 database offers a robust and comprehensive dataset, supporting broad clinical cancer research. The SEER database, while comprehensive, lacks detailed information on comorbidities, which may influence both surgical decisions and survival outcomes. The absence of these data represents a limitation in our analysis, as comorbid conditions can impact a patient's ability to undergo surgery and their subsequent recovery.

Case identification was restricted to those with ovarian anatomical sites, classified based on the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) morphology codes. These codes included 8050, 8120–8122, 8130, 8260, 8290, 8310, 8313, 8380–8383, 8441–8444, 8450, 8460–8463, 8470–8472, 8480–8482, 8570, 9014, and 9015. Inclusion criteria included patients with stage III or IV disease who had undergone surgery or for whom surgery had been recommended but not performed. Exclusion criteria included patients under 50 years of age, those diagnosed solely at the time of death or by autopsy, cases in which the ECO was not the first primary cancer, and individuals without recorded vital status or follow-up data. The cohort was divided into two groups: surgery group and non-surgery group. The Institutional Review Board classified this study as exempt based on the utilization of de-identified data.

Statistical analyses

To address potential confounding factors between the two groups, a Propensity Score Matching (PSM) analysis was conducted. Propensity scores for the two groups were matched using the "Matchit" package in R, which implemented a nearest-neighbor matching algorithm with a 1:2 ratio. Specifically, the matching variables included year of diagnosis, age, race, stage, marital status, median household income, rurality, and chemotherapy. Baseline characteristics between the matched cohorts were then compared using Pearson's Chi-squared test through the "gtsummary" package, with categorical variables presented as proportions and percentages of the total sample.

Overall survival (OS) was defined as the period from diagnosis to all-cause mortality, with survivors censored at their last follow-up date. OS estimates were generated using the Kaplan-Meier method, and differences in OS across cohorts were assessed via log-rank testing. Further subgroup analyses stratified by stage were also conducted.

To examine associations between surgical intervention and OS, multivariable Cox proportional hazards regression models were employed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), adjusting for covariates, including age, year of diagnosis, race, marital status, stage, median household income, rurality, chemotherapy, and surgical status. Additionally, a multivariable logistic regression was performed to model the odds of surgery declination relative to patient characteristics, with adjusted odds ratios (AORs) and 95% CIs reported. Statistical significance was defined as a p-value of < 0.05. All statistical analyses were performed using R software, version 4.3.0 (R Foundation, Vienna, Austria).

Results

A total of 21,988 patients diagnosed with advanced EOC between 2004 and 2021 from the SEER database were included in the final analysis (Figure S1). Of these, 363 patients were in the non-surgery group, while 21,625 were in the surgery group. Within the non-surgery cohort, 256 patients (70.5%) refused surgery, and 104 (29.5%) did not undergo surgery for reasons not specified in the records. The surgery cohort consisted of 19,248 patients (89.0%) who received both surgery and chemotherapy, and 2,377 (11.0%) who underwent surgery alone. Comparative analysis between the non-surgery and surgery groups revealed significant differences in baseline characteristics, including age at diagnosis, race, marital status, stage, median household income, rural residence, and chemotherapy administration. At the end of study, mortality was documented in 326 patients (89.8%) within the non-surgery group and in 14,791 patients (68.4%) within the surgery group (Table 1).

With a median follow-up of 33 months (range, 1–215 months), the observed mean OS was 17.8 months (95% CI, 13.4–22.2 months) for patients in the non-surgery cohort and 45.8 months (95% CI, 41.5–50.1 months) for those in the surgery cohort (log-rank $P < 0.001$; Fig. 1A). Analysis of subgroups revealed mean OS estimates of 13.4 months (95% CI, 11.2–15.6 months) for individuals who declined surgery, 18.2 months (95% CI, 14.2–22.2 months) for patients with unspecified reasons for no surgery, 46.6 months (95% CI, 42.1–51.1 months) for those receiving combined surgery and chemotherapy, and 39.8 months (95% CI, 34.9–44.7 months) for patients who underwent surgical treatment alone (log-rank $P < 0.001$; Fig. 1B).

Following 1:2 PSM, 726 patients in the surgery group were successfully matched to patients in the non-surgery group. Baseline demographic and clinical characteristics were comparable across groups, indicating that PSM effectively mitigated potential selection bias ($P > 0.05$). In the matched cohort, OS was significantly lower among patients in the non-surgery group than those in the surgery group (log-rank $P < 0.001$; Fig. 2). Subgroup analyses further demonstrated that patients in the non-surgery group exhibited consistently lower OS compared with the surgery group for both stage III and stage IV disease, irrespective of PSM adjustment (log-rank $P < 0.001$; Figure S2-3).

The multivariable Cox proportional hazards model identified a significantly increased mortality risk for patients with advanced EOC in the non-surgery group, both before and after PSM (pre-PSM: HR, 2.74; 95% CI, 2.44–3.07; $P < 0.001$; post-PSM: HR, 1.87; 95% CI, 1.62–2.15; $P < 0.001$). Prior to matching, all characteristics included in the model were independent predictors of OS ($P < 0.05$). After matching, year of diagnosis ($P = 0.02$), age at diagnosis ($P < 0.001$), and receipt of chemotherapy ($P < 0.001$) remained significant independent predictors of OS (Table 2).

Multivariable logistic regression analysis showed that Non-Hispanic Black patients (AOR, 1.64; 95% CI, 1.10–2.37) had a higher likelihood of declining surgery than Non-Hispanic White patients. Advanced age was also strongly associated with a greater likelihood of surgery refusal, particularly among those aged 80 years or older (AOR, 11.20; 95% CI, 7.48–16.99). Compared with married patients, those who were divorced (AOR, 1.46; 95% CI, 0.99–2.12), never married (AOR, 1.69; 95% CI, 1.21–2.36), or widowed (AOR, 1.57; 95% CI, 1.19–2.08) demonstrated higher odds of declining surgery. Additionally, lower median household income, stage IV disease, and residence in nonmetropolitan areas were significantly associated with increased odds of surgery refusal (Table 3).

Discussion

The clinical trajectories of patients with advanced EOC who were advised but ultimately did not undergo surgical intervention remain a key area of scholarly and clinical interest. Given ethical constraints, direct examination through randomized controlled trials is not feasible. In such cases, large-scale national databases like the SEER program provide essential resources for research [11–13]. The SEER database, which compiles extensive cancer-related statistics from across the United States, offers researchers critical access to a breadth of data on various malignancies. This resource enables in-depth analyses of clinical outcomes and broader epidemiologic patterns [14].

This retrospective analysis demonstrates marked disparities in survival outcomes between patients with advanced EOC who underwent surgery and those who, despite clinical recommendations, did not proceed with surgery. Adjusted for baseline characteristics using propensity score matching, the non-surgical cohort exhibited significantly reduced OS. The observed differences in survival outcomes emphasize the essential role of cytoreductive surgery in the management of advanced EOC, where it remains the standard of care and is associated with survival benefits across diverse clinical contexts [8, 9]. Evidence suggests that even when cytoreductive surgery is delayed, survival outcomes for patients with advanced EOC may not be adversely affected [15]. Achieving optimal cytoreduction has been consistently

Table 1 Baseline demographics for patients with advanced epithelial ovarian carcinoma, surveillance, epidemiology, and end results (SEER) 17 database, 2004 to 2021

	Before matching			After matching		
Variables	**Non-surgery**	**Surgery**	**P**	**Non-surgery**	**Surgery**	**P**
No. of patients	363	21,625		363	726	
Year of diagnosis			0.41			0.39
2004–2009	120 (33.1)	7,393 (34.2)		120 (33.1)	295 (40.6)	
2010–2015	123 (33.9)	7,768 (35.9)		123 (33.9)	233 (32.1)	
2016–2021	120 (33.1)	6,464 (29.9)		120 (33.1)	198 (27.3)	
Age at diagnosis			< 0.001			0.38
50–59	35 (9.6)	6,752 (31.2)		35 (9.6)	65 (9.0)	
60–69	74 (20.4)	7,822 (36.2)		74 (20.4)	136 (18.7)	
70–79	93 (25.6)	5,410 (25.0)		93 (25.6)	223 (30.7)	
80+	161 (44.4)	1,641 (7.6)		161 (44.4)	302 (41.6)	
Race			0.009			0.88
Non-Hispanic White	267 (73.6)	16,010 (74.0)		267 (73.6)	548 (75.5)	
Non-Hispanic Black	38 (10.5)	1,399 (6.5)		38 (10.5)	69 (9.5)	
Non-Hispanic other	27 (7.4)	1,746 (8.1)		27 (7.4)	47 (6.5)	
Hispanic	31 (8.5)	2,470 (11.4)		31 (8.5)	62 (8.5)	
Marital status			< 0.001			0.39
Married	122 (33.6)	12,380 (57.2)		122 (33.6)	247 (34.0)	
Divorced	39 (10.7)	2,555 (11.8)		39 (10.7)	96 (13.2)	
Never married	58 (16.0)	3,314 (15.3)		58 (16.0)	93 (12.8)	
Widowed	144 (39.7)	3,376 (15.6)		144 (39.7)	290 (39.9)	
Stage			< 0.001			1
III	119 (32.8)	13,686 (63.3)		119 (32.8)	238 (32.8)	
IV	244 (67.2)	7,939 (36.7)		244 (67.2)	488 (67.2)	
Median household income			0.009			0.44
<$59,999	70 (19.3)	2,952 (13.7)		70 (19.3)	133 (18.3)	
$60,000 - $79,999	125 (34.4)	8,469 (39.2)		125 (34.4)	285 (39.3)	
$80,000 - $99,999	114 (31.4)	6,503 (30.1)		114 (31.4)	202 (27.8)	
>$100,000	54 (14.9)	3,701 (17.1)		54 (14.9)	106 (14.6)	
Rurality			< 0.001			0.86
Metropolitan (> 1 million pop)	183 (50.4)	13,334 (61.7)		183 (50.4)	378 (52.1)	
Metropolitan (< 1 million pop)	117 (32.2)	5,956 (27.5)		117 (32.2)	228 (31.4)	
Nonmetropolitan	63 (17.4)	2,335 (10.8)		63 (17.4)	120 (16.5)	
Chemotherapy			< 0.001			1
Yes	165 (45.5)	19,248 (89.0)		165 (45.5)	331 (45.6)	
None/Unknown	198 (54.5)	2,377 (11.0)		198 (54.5)	395 (54.4)	
Vital status						
Alive	37 (10.2)	6,871 (31.2)		37 (10.2)	123 (16.9)	
Died	326 (89.8)	14,791 (68.4)		326 (89.8)	603 (83.1)	
Died from ovarian carcinoma	313	13,618		313	545	
Died from other causes	13	1,173		13	58	

linked to improved prognosis by reducing tumor burden, augmenting the efficacy of adjuvant therapies, and serving as a key predictor of extended OS. While our study focuses on the impact of surgery refusal in advanced EOC, it is important to recognize that non-surgical treatments, such as chemotherapy, targeted therapies, and palliative care, are often employed in patients who are ineligible for surgery or who decline the procedure. These treatments can provide survival benefits, particularly in patients with advanced or metastatic disease. However, research suggests that the survival outcomes for patients receiving non-surgical treatments are generally poorer compared to those who undergo cytoreductive surgery [16].

In the pre-PSM cohort, multivariable Cox proportional hazards analysis identified several factors associated with OS, including surgery, age, year of diagnosis, race, marital status, disease stage, median household income, rural vs. urban residence, and receipt of chemotherapy. Following PSM, surgery, year of diagnosis, age at diagnosis,

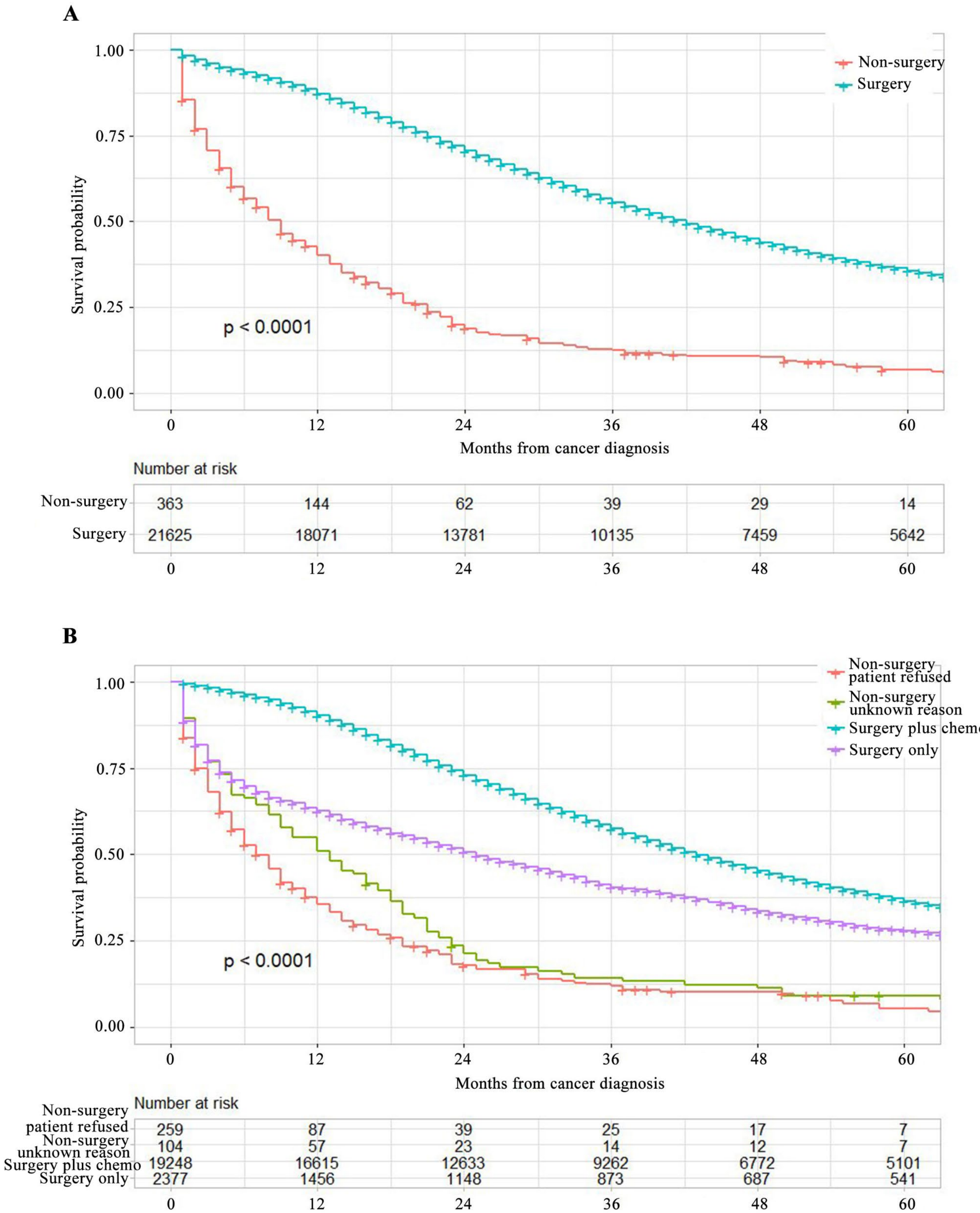

Fig. 1 Kaplan-Meier survival curve of the included patients screened from SEER database. (**A**) non-surgery group versus surgery group (**B**) subgroups

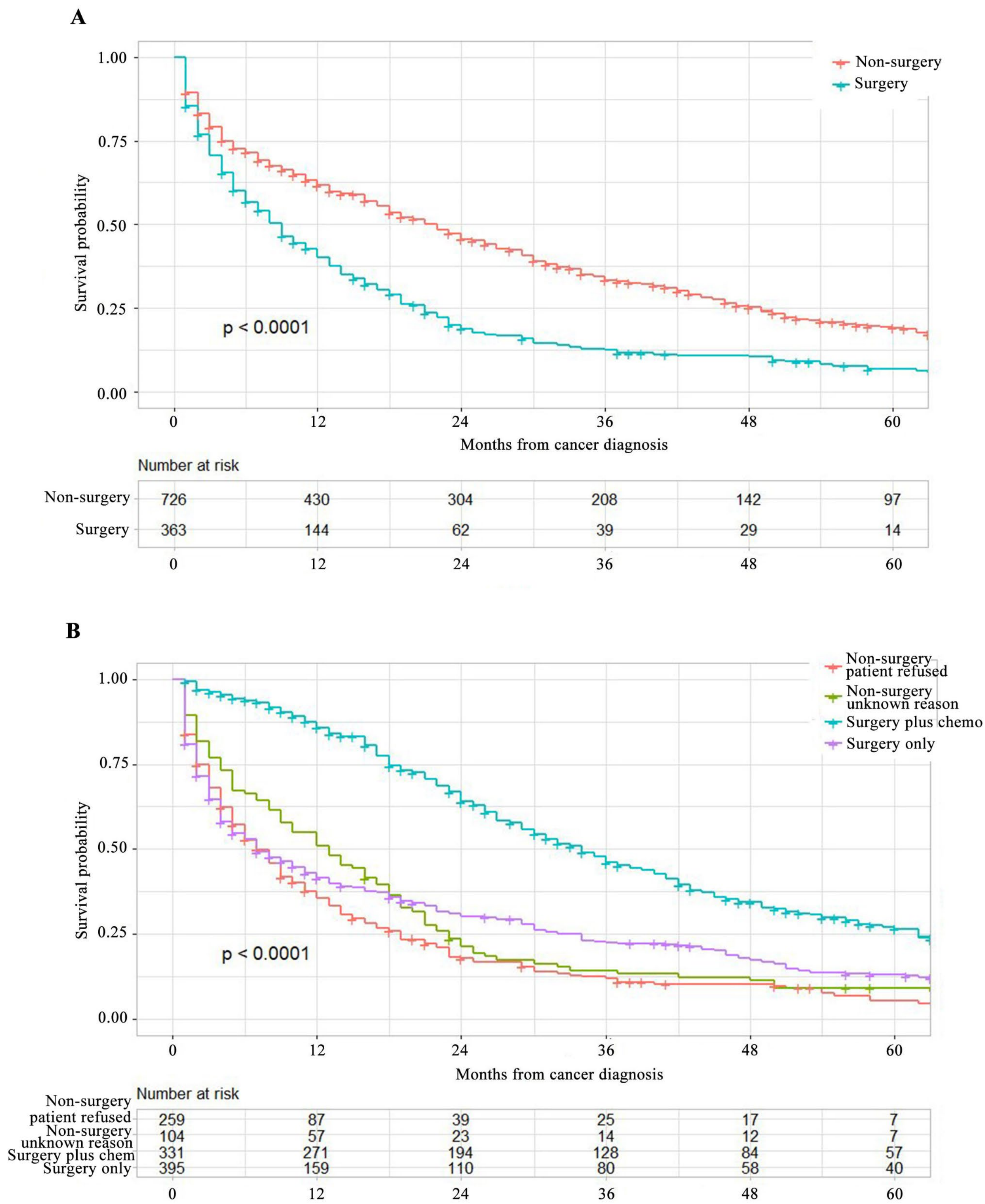

Fig. 2 Kaplan-Meier survival curves of matched cohort. (**A**) non-surgery group versus surgery group (**B**) subgroups

Table 2 Multivariate Cox regression analysis of factors associated with overall survival

Variables	Before matching			After matching		
Year of diagnosis	HR (95% CI)	P	Overall P	HR (95% CI)	P	Overall P
2004–2009	Reference		< 0.001	Reference		0.02
2010–2015	0.88 (0.85–0.92)	< 0.001		0.99 (0.85–1.14)	0.84	
2016–2021	0.77 (0.73–0.81)	< 0.001		0.78 (0.65–0.94)	0.01	
Age at diagnosis			< 0.001			< 0.001
50–59	Reference			Reference		
60–69	1.15 (1.10–1.20)	< 0.001		1.33 (1.01–1.76)	0.04	
70–79	1.39 (1.33–1.46)	< 0.001		1.51 (1.15–1.97)	0.00	
80+	1.91 (1.79–2.04)	< 0.001		1.85 (1.42–2.41)	0.00	
Race			0.04			0.30
Non-Hispanic White	Reference			Reference		
Non-Hispanic Black	1.13 (1.06–1.21)	< 0.001		1.15 (0.92–1.45)	0.22	
Non-Hispanic other	0.90 (0.85–0.96)	< 0.001		0.78 (0.59–1.04)	0.09	
Hispanic	0.97 (0.91–1.02)	0.21		0.94 (0.74–1.19)	0.61	
Marital status			< 0.001			0.82
Married	Reference			Reference		
Divorced	1.11 (1.05–1.16)	< 0.001		1.13 (0.90–1.41)	0.29	
Never married	1.10 (1.05–1.15)	< 0.001		1.13 (0.91–1.41)	0.26	
Widowed	1.10 (1.05–1.15)	< 0.001		0.95 (0.81–1.11)	0.53	
Stage			< 0.001			0.18
III	Reference			Reference		
IV	1.38 (1.34–1.43)	< 0.001		1.09 (0.94–1.26)	0.25	
Median household income			< 0.001			0.34
<$59,999	Reference			Reference		
$60,000 - $79,999	0.92 (0.87–0.97)	< 0.001		0.83 (0.66–1.04)	0.11	
$80,000 - $99,999	0.89 (0.84–0.95)	< 0.001		0.81 (0.64–1.04)	0.10	
>$100,000	0.88 (0.82–0.94)	< 0.001		0.88 (0.66–1.16)	0.36	
Rurality			0.02			0.80
Metropolitan (> 1 million pop)	Reference			Reference		
Metropolitan (< 1 million pop)	1.06 (1.02–1.10)	< 0.001		1.00 (0.85–1.17)	0.96	
Nonmetropolitan	1.03 (0.97–1.10)	0.38		0.92 (0.72–1.18)	0.51	
Chemotherapy			< 0.001			< 0.001
Yes	Reference			Reference		
None/Unknown	1.41 (1.34–1.48)	< 0.001		1.98 (1.72–2.28)	< 0.001	
Group			< 0.001			< 0.001
Surgery	Reference			Reference		
Non-surgery	2.74 (2.44–3.07)	< 0.001		1.87 (1.62–2.15)	< 0.001	

Abbreviations: CI, confidence interval; HR, hazard ratio;

and chemotherapy administration persisted as significant independent predictors of OS. These findings align with prior literature, highlighting the established influence of age [17–19] and chemotherapy [20–22] on survival outcomes. However, Yoshikawa et al. reported no significant differences in overall or disease-free survival between older and younger ovarian cancer patients [23]. It is noteworthy that the conclusions of this study were based on a cohort of 114 Japanese patients with stage I-IV ovarian cancer from a single institution, limiting the generalizability of these findings and warranting cautious interpretation.

This evaluation of sociodemographic influences on surgical decision-making emphasizes the imperative to mitigate barriers limiting access to surgical care [24, 25]. Our study demonstrated that various demographic characteristics—including advanced age, racial and ethnic identity, marital status, and socioeconomic indicators such as income level and rural residency—were significantly associated with a higher incidence of refusal of surgical intervention. Specifically, elderly patients and individuals from lower socioeconomic backgrounds displayed a pronounced tendency to decline surgical intervention, potentially due to concerns surrounding postoperative recovery, limited social support networks, or restricted healthcare access [26–28]. A study by Pinelli C and colleagues demonstrated no significant difference in 30-day morbidity rates between older and younger

Table 3 Sociodemographic and clinicopathologic factors associated with surgery declination: multivariable logistic regression

Variables	AOR (95% CI)	*P*
Year of diagnosis		
2004–2009	Reference	
2010–2015	1.43 (1.08–1.88)	0.01
2016–2021	1.90 (1.43–2.53)	< 0.001
Age at diagnosis		
50–59	Reference	
60–69	1.63 (1.09–2.47)	0.02
70–79	2.68 (1.80–4.06)	< 0.001
80+	11.20 (7.48–16.99)	< 0.001
Race		
Non-Hispanic White	Reference	
Non-Hispanic Black	1.64 (1.10–2.37)	0.01
Non-Hispanic other	1.13 (0.72–1.71)	0.58
Hispanic	0.86 (0.57–1.27)	0.47
Marital status		
Married	Reference	
Divorced	1.46 (0.99–2.12)	0.04
Never married	1.69 (1.21–2.36)	0.002
Widowed	1.57 (1.19–2.08)	0.001
Stage		
III	Reference	
IV	3.75 (2.98–4.74)	< 0.001
Median household income		
<$59,999	Reference	
$60,000 - $79,999	1.03 (0.71–1.51)	0.87
$80,000 - $99,999	1.47 (0.98–2.22)	0.06
>$100,000	1.44 (0.89–2.31)	0.13
Rurality		
Metropolitan (> 1 million pop)	Reference	
Metropolitan (< 1 million pop)	1.67 (1.28–2.17)	< 0.001
Nonmetropolitan	2.40 (1.58–3.60)	< 0.001
Chemotherapy		
Yes	Reference	
None/Unknown	7.53 (5.95–9.53)	< 0.001

Abbreviations: AOR, adjusted odds ratio;

patients with advanced EOC following debulking surgery, indicating that advanced age alone should not preclude the consideration of ultra-radical resection in this population [29].

The observed association between non-Hispanic Black patients and an increased likelihood of surgery refusal highlights potential disparities in healthcare access and delivery, meriting further investigation. Elevated refusal rates among non-Hispanic Black individuals may be influenced by a multifaceted interplay of factors, including systemic distrust in healthcare, historical and ongoing negative experiences with providers, and perceptions of discrimination [30, 31]. Evidence indicates that many Black Americans report adverse interactions with healthcare providers, which may contribute to hesitancy toward surgical interventions [32]. Financial constraints also represent significant obstacles for many Black patients, further limiting access to timely medical care. Although the Affordable Care Act has expanded insurance coverage for certain populations, notable coverage gaps remain, particularly in states that have not adopted Medicaid expansion [33, 34].

Our analysis demonstrates that marital status significantly impacts the likelihood of surgery refusal among patients with advanced EOC. Specifically, divorced, widowed, and never-married individuals showed higher odds of declining surgical intervention compared to married patients. These findings are consistent with existing literature, which highlights the supportive role of marriage in healthcare decision-making, particularly for complex interventions such as surgery [35, 36]. Married patients often benefit from increased social and emotional support, potentially mitigating concerns related to surgery, including fears of postoperative complications and the adequacy of caregiving during recovery [37]. Future research should investigate how marital status shapes patient perspectives on surgical risks and postoperative expectations in the context of advanced EOC.

Patients who declined surgery exhibited significantly reduced OS compared to those who did not undergo surgery due to other, unspecified factors. This suggests that patient-driven decisions to refuse surgery may be influenced by a broader spectrum of non-clinical factors, including psychological, cultural, and systemic considerations. Addressing these factors through comprehensive patient support and education may facilitate more informed and equitable treatment choices [38–40].

Although this study offers valuable insights into factors associated with surgery refusal and its impact on survival outcomes, several limitations warrant consideration. The retrospective study design and the use of SEER database data may introduce selection and reporting biases. Additionally, the absence of detailed information regarding the type of regimen of chemotherapy and specific reasons for surgery refusal, such as comorbidities, limits a comprehensive understanding of patient motivations. Future research should prioritize prospective, multicenter studies to understand patient decision-making and barriers to surgery and develop targeted interventions such as patient navigation programs, financial assistance for underinsured individuals, and culturally sensitive educational campaigns to improve access to surgical care for all patients with advanced EOC.

Declining surgery is associated with significantly poorer survival in advanced EOC. While sociodemographic factors such as age, race, income, and marital status play a key role in surgical decision-making, it is important to recognize that these disparities may be influenced by a combination of factors beyond sociodemographic. Factors such as healthcare access, physician recommendations, cultural influences, and patient preferences may also contribute to the decision to refuse surgery. Addressing these multifactorial determinants is crucial to improving access to surgical care and reducing treatment disparities. Further research with more comprehensive data is needed to explore the complex interplay of these factors and their impact on treatment outcomes in advanced EOC.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-025-03769-3.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Author contributions

Q.Z. conceived and designed the study. L.Z. and G.C. was involved in data acquisition. L.Z., G.C., X.Z., C.X. and M.G. analyzed the data. L.Z. and G.C. wrote the manuscript. Q.Z. revised the manuscript. All authors read and approved the final manuscript.

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Data availability

The data supporting the findings of this study are available upon request from the corresponding author.

Declarations

Ethics approval and consent to participate

None.

Competing interests

The authors declare no competing interests.

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