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Original Article

Surgical outcomes and prognostic factors of neoadjuvant chemotherapy followed by interval debulking surgery in advanced ovarian cancer

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Abstract: Objective: To investigate the surgical outcomes and prognostic factors of neoadjuvant chemotherapy (NACT) combined with interval debulking surgery (IDS) in patients with advanced ovarian cancer. Methods: A retrospective analysis was conducted on clinical data of 97 patients with advanced ovarian cancer admitted to Xijing Hospital of The Fourth Military Medical University from January 2018 to December 2019. The patients were divided into two groups based on their treatment methods: a control group (primary debulking surgery (PDS), n=48) and an observation group (NACT combined with IDS, n=49). Short-term efficacy, perioperative outcomes, tumor markers, immune function, quality of life, adverse reactions, and survival status were compared between the two groups. Factors affecting prognosis were analyzed, a Nomogram prediction model was constructed and validated. Results: The observation group demonstrated superior short-term efficacy than the control group, with lower intraoperative blood loss, shorter hospitalization duration, and reduced transfusion volume ($P<0.05$). After treatment, tumor marker levels, immune function, and quality of life improved significantly in both groups compared to pre-treatment levels, with more pronounced improvements in the observation group ($P<0.05$). The incidence of adverse reactions such as liver injury, kidney injury, nausea and vomiting, and myelosuppression was lower in the observation group than in the control group ($P<0.05$). Additionally, no significant difference in 5-year progression-free survival (PFS) and overall survival (OS) was observed between the two groups ($P>0.05$). Univariate and multivariate regression analyses identified age ≥50 years, tumor size >10 cm, low differentiation, PDS, and presence of residual lesions as independent prognostic factors. The Nomogram prediction model achieved an AUC of 0.955 (95% CI: 0.917-0.993), with calibration curves closely aligning with the ideal line, indicating high predictive accuracy and reliability. Conclusion: NACT combined with IDS demonstrated superior short-term efficacy compared to traditional PDS in patients with advanced ovarian cancer, with improved perioperative conditions, reduced adverse reactions, and enhanced survival rates. Age, tumor size, histological differentiation, and treatment modality independently affect patient prognosis. The Nomogram prediction model developed in this study demonstrates excellent discriminative power and clinical applicability for prognostic evaluation.

Keywords: Ovarian cancer, neoadjuvant chemotherapy, interval debulking surgery, prognostic factors

Introduction

Ovarian cancer is one of the most common gynecologic malignancies in clinical practice, with the highest mortality rate among gynecologic tumors [1]. Approximately 70% of patients are diagnosed at advanced stages due to insidious symptom onset and rapid disease progression [2]. The current standard treatment is primary debulking surgery (PDS) followed by chemotherapy. However, in cases with extensive tumor burden or widespread metastasis, PDS often fails to achieve optimal cytoreduction [3], highlighting the need for alternative treatment strategies.

Neoadjuvant chemotherapy (NACT) before interval debulking surgery (IDS) offers a new approach. NACT, typically administered for two to three cycles before surgery, shrinks tumor volume, eradicates micrometastases, alleviates ascites, and facilitates surgical resection [4]. While this regimen improves surgery success, its long-term benefits remain unclear.

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Further studies are required to clarify surgical outcomes and prognostic factors associated with this strategy.

This study aimed to evaluate the efficacy of NACT combined with IDS in patients with advanced ovarian cancer, identify prognostic factors, and develop a Nomogram predictive model. These findings may assist clinicians in optimizing individualized treatment strategies and improving patient outcomes.

Materials and methods

Experimental design

This retrospective study analyzed clinical data from 97 patients with advanced ovarian cancer treated at Xijing Hospital, The Fourth Military Medical University, from January 2018 to December 2019. The patients were divided into two groups based on the treatment methods: the control group (PDS, n=48) and the observation group (NACT combined with IDS, n=49). This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of The Fourth Military Medical University (No. KY20252224-F-1).

Diagnostic criteria: The diagnosis of ovarian cancer was based on the *Guidelines for the Diagnosis and Treatment of Ovarian Cancer (2018 Edition)* [5]. Tumor staging followed the criteria of the International Federation of Gynecology and Obstetrics (FIGO) [6, 7].

Inclusion criteria: 1) histopathologically and clinically confirmed advanced ovarian cancer (FIGO Stage IIIc-IV); 2) primary ovarian cancer at initial diagnosis and treatment; 3) absence of other organic diseases involving the heart, lungs, or other organs; 4) tolerance to anesthesia and surgery; 5) no prior history of related surgeries; 6) no hematologic disorders or infectious diseases; 7) no surgical contraindications based on performance status; and 8) availability of complete clinical and follow-up data.

Exclusion criteria: 1) non-primary ovarian cancer; 2) concurrent malignancies; 3) radiological evidence of lungs, liver, or other distant metastasis; 4) severe psychiatric disorders; or 5) incomplete clinical data or those lost to follow-up.

Surgical methods

Observation group: Patients in the observation group received NACT followed by IDS. The specific regimen included: (1) paclitaxel (H2008-3850; Haikou Pharmaceutical Factory Co., Ltd., China) at a dose of 135-175 mg/m^2, administered intravenously over 3 hours on Day 1; (2) carboplatin (H20040813; Jiangsu Hansoh Pharmaceutical Co., Ltd., China), dosed according to an area under the curve (AUC) of 5-6, administered intravenously over 1 hour. Cycles were repeated every 21 days.

After NACT, patients underwent clinical reassessment using physical examination and ancillary investigations. IDS was performed after an average of three cycles of NACT. The surgical scope included total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, and removal of pelvic and peritoneal metastases as well as any grossly visible lesions. Postoperatively, patients received 6-8 additional cycles of chemotherapy with the same paclitaxel-carboplatin regimen.

Control group: Patients in the control group underwent PDS directly, with the same surgical procedures as IDS. Postoperatively, they also received 6-8 cycles of chemotherapy, administered in the same manner as in the observation group.

Observation index and evaluation of curative effect

Baseline characteristics: Baseline data included age, FIGO stage, tumor differentiation grade.

Short-term efficacy: Short-term efficacy was evaluated at four weeks after completion of the last chemotherapy. All patients underwent abdominal and pelvic MRI, CT, and ultrasound examinations. Therapeutic efficacy was evaluated according to the World Health Organization (WHO) criteria for solid tumor response assessment and the Gynecologic Cancer Intergroup (GCIG) criteria for ovarian cancer [8]. Complete response (CR): complete disappearance of all tumor lesions or ascites for more than 4 weeks; Partial response (PR): reduction in tumor volume or ascites by ≥50% for more than 4 weeks; Stable disease (SD): no significant change in tumor volume or ascites; Progressive disease

(PD): increase in tumor volume or ascites with clinical deterioration.

Perioperative outcomes: Parameters evaluated included surgical time, intraoperative blood loss, intraoperative blood transfusion volume, and hospitalization duration.

Tumor markers: Fasting venous blood (5 mL) was collected from each patient in the early morning before and after treatment. Blood samples were centrifuged at 1500 r/min for 15 minutes, and the supernatant was used for analysis. Serum levels of carbohydrate antigen 125 (CA125, MLBio, China), human epididymal protein 4 (HE4, CUSABio), and vascular endothelial growth factor (VEGF, DAKEWE, China) were measured using enzyme-linked immunosorbent assay (ELISA).

Immune function: The proportions of $CD4^+$, $CD3^+$, and $CD8^+$ in peripheral venous blood were detected by flow cytometry (Thermo Fisher, China), and the ratio of $CD4^+/CD8^+$ was calculated.

Quality of life: Quality of life was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [9], focusing on five dimensions: physical, emotional, social, cognitive, and role functioning. Each dimension was scored on a 100-point scale, with higher scores indicating better quality of life.

Adverse reactions: Adverse reactions, including liver and kidney injury, nausea and vomiting, and myelosuppression were evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (NCI CTCAE) 3.0 [10]. Grade I: mild; asymptomatic or requiring only clinical observation without intervention; Grade II: moderate; requiring pharmacologic or local intervention; Grade III: severe; requiring systemic treatment or intervention, affecting daily living; Grade IV: life-threatening; requiring urgent intervention and possible hospitalization); Grade V: death.

Survival status: Five-year progression-free survival (PFS) and 5-year overall survival (OS) were recorded for both groups. PFS was defined as the time from treatment completion to documented tumor progression (e.g., increased tumor volume or ascites, clinical deterioration). Patients were followed up via telephone or outpatient visits. For the first two years, follow-ups were conducted every three months, and then every six months, until five years after the surgery.

Statistical methods

SPSS 23.0 and GraphPad Prism 8.0 were used for data analysis and graphic drawing. Quantitative variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were expressed as mean ± standard deviation, and the inter-group comparisons were conducted using independent sample t test (two group comparison) or one-way analysis of variance (ANOVA) combined with post-hoc LSD or Tukey method (multiple groups); non-normally distributed data were expressed as median (interquartile range), and the inter-group comparisons were conducted using Mann-Whitney U test (two groups) or Kruskal-Wallis H test (multiple groups). Categorical variables were analyzed using the Pearson chi-square test or Fisher's exact test (if expected frequencies were <5).

Survival analysis was performed using the Kaplan-Meier method, intergroup differences were evaluated using the log-rank test. Prognostic factors were initially screened by univariate analysis ($P<0.05$), followed by multivariate Logistic proportional hazards regression analysis to identify independent prognostic factors. A Nomogram prediction model was constructed based on the results of multivariate analysis results. Model performance was verified using the receiver operating characteristic (ROC) curve for discrimination (area under the curve, AUC), calibration curve combined with Hosmer-Lemeshow test for calibration, and decision curve analysis (DCA) for clinical utility evaluation. All statistical tests were two-sided, and $P<0.05$ was considered statistically significant.

Results

Baseline characteristics

There were no significant differences in the baseline characteristics between the two groups ($P>0.05$), indicating comparability (**Table 1**).

Table 1. Comparison of baseline characteristics between the two groups

	Control group (n=48)	Observation group (n=49)	χ^2	*P* value
Age, years			2.313	0.128
<50	21	29		
≥50	27	20		
FIGO			0.523	0.470
IIIc	31	35		
IV	17	14		
Degree of differentiation			0.856	0.652
Low differentiation	13	17		
Moderate differentiation	15	12		
High differentiation	20	20		

Note: FIGO = International Federation of Gynecology and Obstetrics.

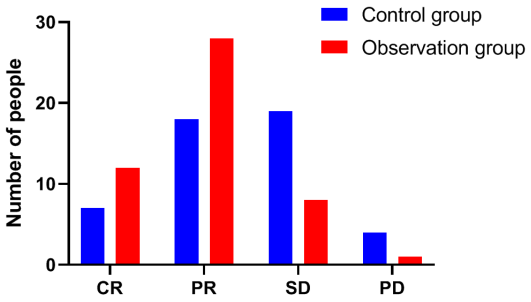

Figure 1. Comparison of short-term efficacy between the two groups. CR = Complete response; PR = Partial response; SD = Stable disease; PD = Progressive disease.

Short-term efficacy

In the observation group, 12 patients achieved CR and 28 achieved PR. In the control group, 7 patients achieved CR and 18 achieved PR. The short-term efficacy rate in the observation group was 81.63%, significantly higher than 52.08% of the control group (χ^2=6.618, *P*= 0.010) (**Figure 1**).

Perioperative outcomes

All patients in both groups successfully completed surgery. Surgical time, intraoperative blood loss, and transfusion volume were significantly lower in the observation group compared to the control group (*P*<0.05). However, there was no significant difference in hospitalization duration between the two groups (*P*>0.05) (**Table 2**).

Tumor markers

Serum levels of CA125, HE4, and VEGF were significantly decreased after treatment in both groups (all P<0.05). Notably, the observation group demonstrated significantly lower levels than those in the control group (all *P*<0.05) (**Figure 2**).

Immune function

Immune function indicators, including $CD3^+$, $CD4^+$, $CD8^+$, and the $CD4^+/CD8^+$ ratio, were significantly improved in both groups after treatment compared to pre-treatment levels, with the observation group showing more pronounced improvements than the control group (*P*<0.05) (**Figure 3**).

Quality of life

After treatment, scores on all dimensions of the EORTC QLQ-C30 significantly increased in both groups compared to their baseline level. The observation group exhibited significantly greater improvements than the control group (*P*<0.05), with the most notable gains observed in social functioning and role functioning (*P*<0.05). See **Table 3**.

Adverse reactions

No Grade IV or V adverse reactions occurred in either group. In the control group, the incidence of Grade II-III adverse reactions, including hepatic injury, nausea and vomiting, and myelosuppression, was higher. No significant difference was observed in cardiotoxicity between the two groups (*P*>0.05). The severity of hepatic and renal injury, nausea and vomiting, and myelosuppression was significantly lower in the observation group compared with the control group (*P*<0.05) (**Table 4**).

Table 2. Comparison of perioperative outcomes between the two groups [mean ± SD]

	Control group (n=48)	Observation group (n=49)	*t*	*P* value
Surgical time/min	210.21±37.59	153.45±32.92	7.916	<0.001
Intraoperative blood loss/mL	571.42±259.07	428.36±202.92	3.031	0.003
Intraoperative blood transfusion/mL	419.27±280.15	293.39±170.03	2.682	0.009
Hospitalization duration/d	13.48±5.65	12.10±6.62	1.103	0.273

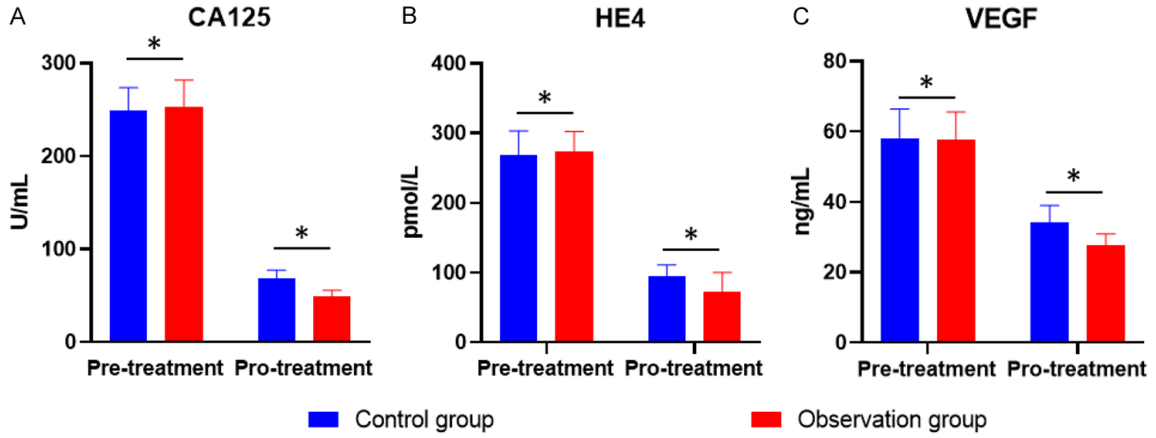

Figure 2. Comparison of tumor marker levels between the two groups. A. CA125; B. HE4; C. VEGF. *P<0.05. CA125 = Carbohydrate antigen 125; HE4 = Human epididymal protein 4; VEGF = Vascular endothelial growth factor.

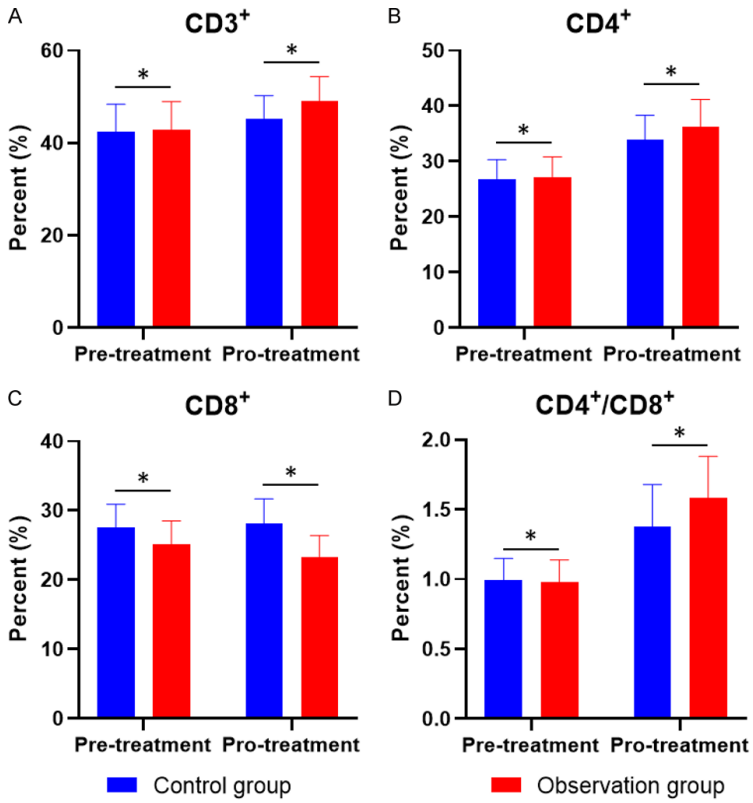

Figure 3. Comparison of immune function between the two groups. A. $CD3^+$; B. $CD4^+$; C. $CD8^+$; D. $CD4^+/CD8^+$. *P<0.05.

Survival analysis

At the end of follow-up (60-month period), the control group demonstrated a 5-year PFS rate of 10.42% and a median PFS of 36 months, while the 5-year OS rate and median OS were 22.92% and 39 months, respectively. In the observation group, the 5-year PFS rate and median PFS were 18.37% and 35 months, respectively, while the 5-year OS rate and median OS were 40.82% and 44 months, respectively. No significant differences in PFS or OS were observed between the two groups (*P*>0.05) (**Figure 4**).

Univariate analysis of prognostic factors

Patients were reclassified into survival and death groups based on follow-up outcomes. Univariate analysis revealed statistically significant differ-

Table 3. Comparison of quality of life between the two groups [mean ± SD]

		Control group (n=48)	Observation group (n=49)	*t*	*P* value
Social functioning	Pre-	43.40±9.85	42.92±9.04	0.250	0.804
	Pro-	65.83±10.48*	73.98±11.26*	3.689	<0.001
Physical functioning	Pre-	40.13±8.88	41.06±10.45	0.472	0.636
	Pro-	68.17±11.92*	86.20±12.13*	7.382	0.001
Role functioning	Pre-	39.23±6.42	39.65±7.13	0.305	0.759
	Pro-	61.73±9.21*	68.88±9.98*	3.624	<0.001
Cognitive functioning	Pre-	41.25±8.36	40.84±7.92	0.248	0.803
	Pro-	61.13±12.02*	68.73±11.81*	3.141	0.002
Emotional functioning	Pre-	44.75±10.22	43.80±10.24	0.457	0.647
	Pro-	66.08±13.46*	72.80±13.58*	0.447	0.016

Note: Compared with the same group before treatment, *P<0.05.

Table 4. Comparison of the incidence of adverse reactions between the two groups [n (%)]

	Control group (n=48)	Observation group (n=49)	χ^2	*P* value
Cardiotoxicity			0.136	0.713
Grade I and below	42 (87.50)	45 (91.84)		
Grade II-III	6 (12.50)	4 (8.16)		
Hepatic injury			8.908	0.003
Grade I and below	34 (70.83)	46 (93.88)		
Grade II-III	14 (29.17)	3 (6.12)		
Renal injury			4.037	0.045
Grade I and below	37 (77.08)	45 (91.84)		
Grade II-III	11 (22.92)	4 (8.16)		
Nausea and vomiting			4.571	0.033
Grade I and below	35 (72.92)	44 (89.80)		
Grade II-III	13 (27.08)	5 (10.20)		
Myelosuppression			6.149	0.013
Grade I and below	32 (66.67)	43 (87.76)		
Grade II-III	16 (33.33)	6 (12.24)		

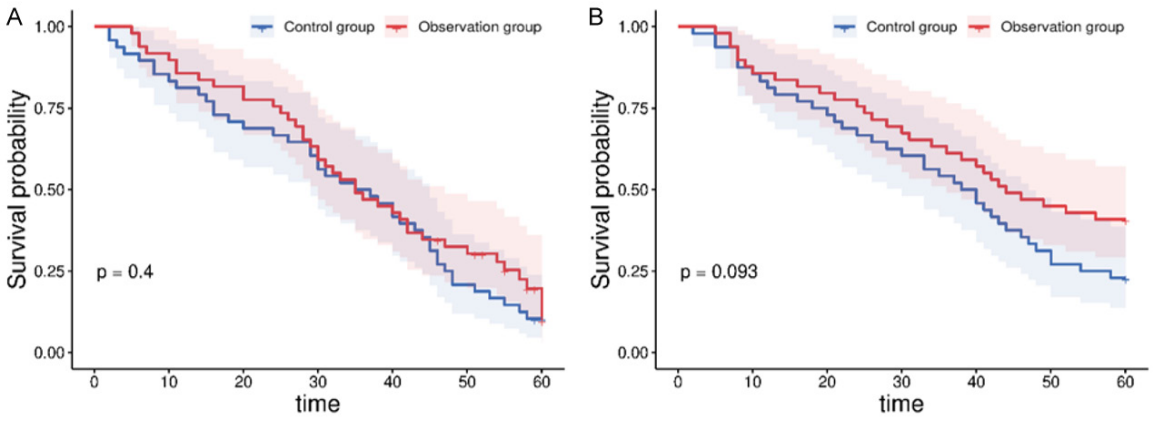

Figure 4. Comparison of survival status between the two groups. A. Progression-free survival; B. Overall survival.

ences between the two groups in terms of age, clinical stage, tumor size, differentiation grade, surgical approach, residual lesions, and number of chemotherapy cycles (*P*<0.05) (**Table 5**).

Table 5. Univariate analysis of poor prognosis in patients with advanced ovarian cancer

Variables		Number of cases (survive/Death)	*P*	*OR*	95% *CI*
Age	<50	25/25			
	≥50	6/41	<0.001	6.833	2.463-18.958
Clinical stage	III	23/43			
	IV	8/23	0.375	1.538	0.594-3.978
Tumor size	<5 cm	17/9			
	5-10 cm	12/23	0.018	3.620	1.245-10.530
	>10 cm	2/34	<0.001	32.111	6.235-165.378
Degree of differentiation	Low differentiation	16/14			
	Moderate differentiation	8/19	0.074	2.714	0.909-8.105
	High differentiation	7/33	0.002	5.388	1.818-15.963
Surgical procedures	NACT combined with IDS	23/20			
	PDS	8/46	<0.001	6.613	2.530-17.281
Residual lesions	No	21/17			
	≤1 cm	6/31	<0.001	6.382	2.161-18.852
	>1 cm	4/18	0.008	5.559	1.580-19.559
Number of chemotherapy sessions	≥8 times	21/30			
	<8 times	10/36	0.043	2.520	1.029-6.170

Note: NACT = Neoadjuvant chemotherapy; IDS = Interval debulking surgery; PDS = Primary debulking surgery.

Table 6. Multivariate analysis of poor prognosis in patients with advanced ovarian cancer

Diagnostic trait		*β*	*S.E.*	*Z*	*P*	*OR*	95% *CI*
Age	<50						
	≥50	1.836	0.736	2.408	0.016	6.273	1.407-27.970
Tumor size	<5 cm						
	5-10 cm	1.332	0.789	1.689	0.091	3.788	0.808-17.766
	>10 cm	2.723	1.025	2.656	0.008	15.227	2.041-113.599
Degree of differentiation	High differentiation						
	Moderate differentiation	1.863	0.976	1.908	0.056	6.446	0.951-43.695
	Low differentiation	2.938	0.949	3.095	0.002	18.874	2.936-121.313
Surgical Procedures	NACT combined with IDS						
	PDS	2.133	0.752	2.836	0.005	8.840	1.933-36.854
Residual lesions	No						
	≤1 cm	1.625	0.822	1.976	0.048	5.079	1.014-25.446
	>1 cm	2.074	0.951	2.180	0.029	7.956	1.233-51.325
Number of chemotherapy sessions	≥8 times						
	<8 times	1.035	0.728	1.421	0.115	2.815	0.675-11.735

Note: NACT = Neoadjuvant chemotherapy; IDS = Interval debulking surgery; PDS = Primary debulking surgery.

Multivariate analysis of prognostic factors

Variables with statistical significance in the univariate analysis were included in the multivariate analysis, with survival status as the dependent variable (death =1, survival =0). Multivariate analysis identified the following as independent risk factors for poor prognosis: age ≥50 years (*OR*=6.273, 95% *CI*: 1.407-27.970), tumor size >10 cm (*OR*=15.227, 95% *CI*: 2.041-113.599), low differentiation (*OR*=18.874, 95% *CI*: 2.936-121.313), PDS (*OR*=8.840, 95% *CI*: 1.933-36.854), and residual lesions >1 cm (*OR*=7.956, 95% *CI*: 1.233-51.325) (**Table 6**).

Construction of a nomogram prediction model

Based on these prognostic factors, a Logistic regression-based risk prediction model was

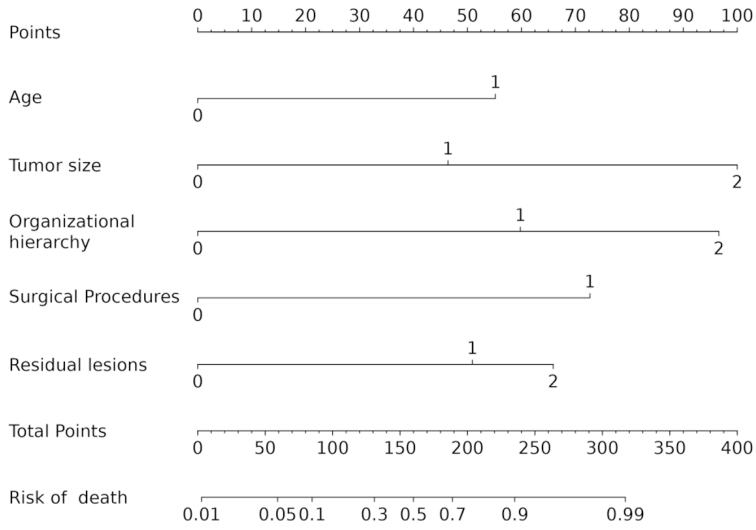

Figure 5. The Nomogram-based prediction model.

constructed using the following formula: log (*P*) =1.836 × Age + 1.332 or 2.723 × Tumor size + 2.938 × Differentiation + 2.133 × Surgical Procedures + 1.625 or 2.074 × Residual lesions. A Nomogram was subsequently developed to assign scores for each prognostic factor (**Figure 5**).

Validation of the nomogram prediction model

The nomogram achieved an AUC of 0.932 (95% CI: 0.880-0.984), demonstrating good discriminative ability, as shown in **Figure 6A**. The nomogram model was internally validated using the Bootstrap method, and its accuracy was assessed using calibration curves. Results showed that the calibration curve fit well with the ideal curve, indicating good agreement between predicted and actual outcomes, as shown in **Figure 6B**. DCA further confirmed the clinical utility of the model across a wide range of threshold probabilities (**Figure 6C**).

Discussion

Approximately 80% of patients with ovarian cancer respond well to platinum-based chemotherapy [11], which forms the foundation of treatment for advanced disease. In the 1970s, Griffiths et al. first introduced NACT, demonstrating that it reduces tumor burden and facilitates subsequent surgery [12]. NACT is especially advantageous in cases where tumors extend to the upper abdomen or thoracic cavity, which makes PDS technically challenging or unsafe. Therefore, NACT offers a safe alternative and may improve surgical outcomes. However, debate continues. Some studies suggest that NACT favorably alters tumor biology and improves survival [13], whereas others warn that NACT may induce chemoresistance. Furthermore, the extent of surgery after NACT is still debated [14].

In this study, the observation group received NACT followed by IDS achieved a significantly higher short-term response rate of 81.63%, compared with the control group treated with PDS (52.08%), consistent with findings reported by Machida et al. [15]. The advantages of the NACT-IDS approach are multifaceted. Preoperative chemotherapy markedly reduces tumor size: Paclitaxel inhibits microtubule depolymerization, arresting cells in mitosis [16], while carboplatin induces DNA adduct formation and triggers apoptosis [17, 18]. Reduced tumor burden facilitates surgical exposure, improves the likelihood of complete cytoreduction (R0 resection) - a critical prognostic factor [19], and decreases operative time, blood loss, transfusion requirements, and hospitalization duration, thereby lowering perioperative morbidity and costs [20]. Additionally, cytoreductive surgery following NACT removes bulky, poorly perfused tumors, leaving smaller nodules with improved vascularization [21]. Enhanced perfusion promotes chemotherapeutic drug penetration, while accelerated cell cycling increases tumor cell susceptibility to subsequent chemotherapy [22]. Trials such as EORTC 55971 [23] and CHORUS [24] have corroborated these benefits, reporting higher complete resection rates and better quality of life in patients undergoing NACT-IDS.

Tumor markers are useful valuable indicators of treatment response in ovarian cancer. CA125, a high-molecular weight glycoprotein expressed on ovarian cancer cells and detectable in serum, remains the most widely used biomarker for diagnosis, treatment monitoring, and prognostication [25]. HE4, a more recently identified biomarker, demonstrates high specificity for ovarian cancer and is particularly infor-

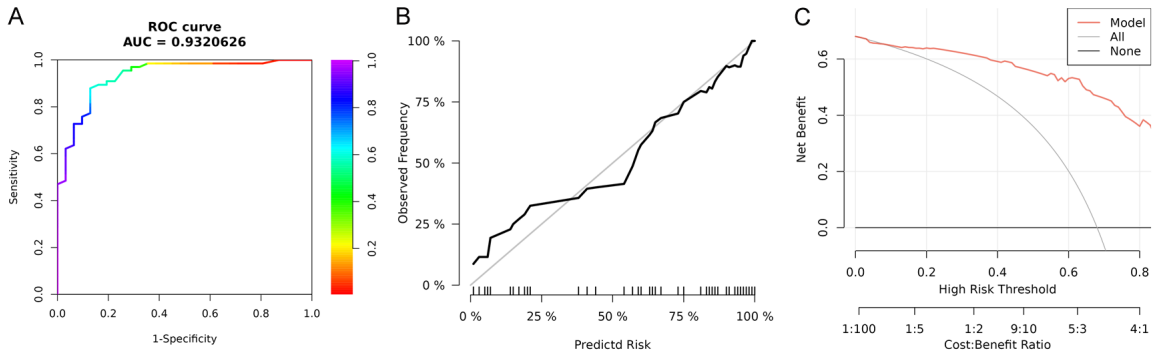

Figure 6. Validation of the nomogram-based prediction model. A. ROC curve; B. Calibration curve; C. DCA curve.

mative even in early-stage disease [26]. A marked post-treatment decline in HE4 usually signals favorable outcomes, whereas persistently elevated levels may predict relapse or treatment failure. In our cohort, both CA125 and HE4 decreased significantly following NACT-IDS. This decline can be attributed to three interconnected mechanisms. First, chemotherapy reduces tumor burden: paclitaxel arrests cells in mitosis, while carboplatin induces apoptosis through DNA adduct formation [27, 28]. Consequently, fewer viable tumor cells release these biomarkers. Second, IDS physically removes residual tumor tissue, directly reducing the number of CA125- and HE4-producing cells [29]. Third, surgical cytoreduction alleviates tumor-associated immunosuppression, restoring immune surveillance and promoting clearance of residual malignant cells [30]. Together, these mechanisms explain the marked reduction in serum CA125 and HE4 observed post-treatment and underscore their value as biological readouts of therapeutic efficacy.

VEGF is a key regulator of tumor angiogenesis. It promotes vascular permeability, degrades the extracellular matrix, and drives endothelial cell proliferation and migration, ultimately fostering neovascularization [31]. In normal tissue, pro- and anti-angiogenic signals are balanced, maintaining vascular stability. Tumors break this balance, with pro-angiogenic signals predominating and resulting in aberrant, immature vasculature [32]. Hypoxia is the principal trigger for this process. Low oxygen tension stabilizes HIF-1α in tumor cells, which binds to the VEGF promoter and markedly increases VEGF transcription. In our study, VEGF levels declined significantly following NACT-IDS. This effect can be attributed to two main mechanisms. First, NACT reduces tumor burden, alleviating extrinsic pressure on adjacent vasculature, improving blood flow and oxygenation, thereby attenuating HIF-1α activation and suppressing VEGF transcription [33, 34]. Second, IDS eliminates large tumor masses, removing VEGF-producing cells and disrupting the tumor microenvironment (TME). This resection reduces local pro-angiogenic signals, further decreasing VEGF production [35]. Collectively, NACT plus IDS effectively mitigates tumor-driven angiogenesis.

The TME functions as a dynamic ecosystem comprising tumor cells, immune cells, cancer-associated fibroblasts (CAFs), endothelial cells, ECM, and cytokines [36]. These components interact through direct contact and soluble mediators, collectively orchestrating tumor initiation, progression, and therapeutic resistance. T cells are critical immune effectors within this milieu, with $CD3^+$, $CD4^+$, and $CD8^+$ subsets playing distinct roles: $CD4^+$ cells coordinate immune responses via cytokine secretion, while $CD8^+$ cells exert direct cytotoxicity against tumor cells [36]. However, tumors evade immunity by releasing suppressive factors that induce T-cell exhaustion, characterized by reduced $CD3^+$ and $CD4^+$ cell levels, elevated $CD8^+$ levels, and a decreased $CD4^+/CD8^+$ ratio [37]. In our study, NACT-IDS significantly improved immune indices. Similar findings were reported by Cao et al. [38], who demonstrated that NACT-IDS not only reduces tumor burden and but also remodels the TME, reversing immune suppression and enhancing T-cell activity. This immunological restoration may contribute to improved therapeutic efficacy and survival outcomes [39].

Ovarian cancer imposes substantial physical and psychological burdens. Ascites, bowel obstruction, abdominal pain, and dyspepsia limit physical functioning [40]. Although chemotherapy reduces tumor burden, it also causes nausea, vomiting, fatigue, and hair loss, adversely affecting physical and mental health and contributing to anxiety and depression [41]. The NACT-IDS offers a more balanced strategy. By reducing tumor bulk preoperatively [42], NACT alleviates vascular and organ compression, mitigating hypoxia, chronic pain, and metabolic disturbances [43]. Improved physical health facilitates psychosocial recovery, enabling patients to resume family and occupational roles [44]. In contrast, PDS is more extensive, leading to greater postoperative weakness and necessitating higher-intensity adjuvant chemotherapy. This increases the risk of hepatic dysfunction, gastrointestinal toxicity, and myelosuppression [45]. By reducing tumor burden before surgery, NACT-IDS allows for less extensive surgery, reduces perioperative trauma, preserves immune function, and lowers the incidence of Grade II-III toxicities. Overall, this strategy mitigates suffering, enhances treatment tolerance, and improves quality of life.

Despite these perioperative and short-term benefits, the impact of NACT-IDS on long-term survival remains controversial. In this study, no significant difference in 5-year PFS or OS were observed between the two groups, aligning with the ongoing debate in the literature. Meta-analyses of EORTC 55971 and CHORUS trials demonstrated survival benefits in select populations, particularly Stage IV patients and those with high-burden Stage IIIC disease, often older individuals with extensive tumor spread [46]. Conversely, other studies indicate that younger Stage III patients with low tumor burden may derive greater benefit from primary PDS [47]. Vergote et al. also cautioned that NACT could promote platinum resistance and early relapse, potentially negating the survival advantages of complete cytoreduction [23]. Reflecting this complexity, current NCCN guidelines continue to recommend PDS plus adjuvant chemotherapy as the standard of care, reserving NACT for carefully selected patients with unresectable disease or poor surgical candidates [48, 49].

This study utilized univariate and multivariate analyses to identify key prognostic factors in advanced ovarian cancer, including age ≥50 years, tumor size >10 cm, low histological differentiation, PDS approach, and residual lesions. These factors cover patient characteristics, tumor biology, and treatment strategies, all of which impact long-term survival and prognosis. Age-related decline in physiological reserve and immune competence may partly explain the poorer prognosis observed in older patients. Immunosenescence reduces the ability to recognize and eliminate malignant cells, impairing host defense against tumor invasion and metastasis [50, 51]. Tumor size reflects the overall disease burden; larger tumors are more likely to invade nearby tissues and organs, complicating complete surgical resection and increasing the likelihood of residual disease, which predisposes to recurrence and worsens survival [52]. Moreover, larger tumors are typically more vascularized, facilitating nutrient delivery, rapid growth, and further dissemination [53]. Histological differentiation is an important marker of tumor aggressiveness. Poorly differentiated tumors exhibit accelerated proliferation, enhanced metastatic potential, and relative resistance to conventional chemotherapy, contributing to unfavorable clinical outcomes [54]. Surgical approach profoundly influences patient outcomes. In our study, patients undergoing PDS demonstrated poorer prognoses. Several factors may contribute to this finding. First, in cases with extensive tumor burden, complete cytoreduction during PDS is technically challenging, increasing the likelihood of residual disease postoperatively. Second, PDS is associated with higher perioperative morbidity, which may delay or compromise the delivery and efficacy of subsequent chemotherapy. Third, extensive surgical trauma may alter the tumor microenvironment in ways that facilitate recurrence and metastatic spread [55]. In contrast, NACT-IDS offers preoperative tumor shrinkage, thereby simplifying surgical resection and improving safety. However, NACT may also induce platinum resistance, adversely affecting long-term survival [56]. Importantly, residual disease remains a critical determinant of prognosis regardless of surgical approach. Residual tumor cells can disseminate via hematogenous or lymphatic pathways, leading to distant metastases [57]. Studies have confirmed that the size of residual lesions strongly correlates with recurrence risk and survival duration [58]. Therefore, surgical

decision-making must be individualized, considering tumor burden, patient performance status, and treatment tolerance.

In this study, multivariate analysis identified five independent prognostic factors, including age, tumor size, differentiation grade, surgical procedures, and residual lesions. Subsequently, a nomogram-based predictive model was constructed for visualized risk assessment. This model demonstrated notable advantages and innovations in predicting postoperative recurrence in patients with advanced ovarian cancer. First, the model demonstrated excellent discriminatory power, with an AUC of 0.932, indicating high accuracy in stratifying recurrence risk. Additionally, the calibration curve showed good agreement with the ideal curve, confirming strong concordance between predicted and observed outcomes and underscoring the model's reliability and stability. Second, the nomogram translates complex risk factors into an intuitive format, enabling individualized recurrence risk prediction. This visualization enhances clinical interpretability and usability, enabling physicians to incorporate risk stratification into routine practice. In clinical practice, this model can help clinicians identify high-risk patients, guiding tailored postoperative management. It can inform decisions regarding the intensity and frequency of adjuvant therapy, ultimately improving patient survival and quality of life.

Several limitations of this study should be acknowledged. First, its retrospective design may have introduced selection bias and limited control over potential confounding factors. Second, the relatively small sample size and single-center setting may affect the robustness and generalizability of the results. Third, emerging therapeutic modalities, such as targeted agents and immunotherapies, were not incorporated into the analysis; thus, direct comparisons between NACT-IDS and these novel approaches remain lacking.

These limitations underscore the need for future research. Large-scale, multicenter prospective studies with longer follow-up are warranted to validate our findings and further define the role of NACT-IDS in the comprehensive treatment of advanced ovarian cancer. Additionally, integrating molecular markers and novel therapies into predictive models may enhance individualized treatment strategies and improve patient outcomes.

Conclusions

This study evaluated NACT combined with IDS in advanced ovarian cancer and demonstrated clear benefits in both short-term and long-term outcomes. In the short term, this approach enhanced tumor control, optimized surgical conditions, and improved quality of life. Long-term follow-up suggested potential survival advantages, supporting NACT-IDS as a valuable option for advanced ovarian cancer patients. A nomogram prediction model was established using key prognostic factors, enabling more accurate recurrence risk assessment and facilitating personalized treatment planning. Additionally, dynamic monitoring of tumor markers and immune function provided reliable indicators of treatment response, offering a basis for timely treatment adjustments.

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Disclosure of conflict of interest

None.

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