

Original Article

Survival outcomes, treatment response, and prognostic factors of different treatment modalities in patients with epithelial ovarian cancer: a retrospective cohort study

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Abstract: Epithelial ovarian cancer (EOC) is commonly diagnosed at an advanced stage; however, the optimal upfront treatment - primary debulking surgery (PDS) versus neoadjuvant chemotherapy followed by interval debulking surgery (NACT+IDS) - remains controversial. This single-center retrospective cohort study used propensity score matching (PSM) to compare overall survival (OS), progression-free survival (PFS), surgical outcomes, tumor response, and safety between PDS and NACT+IDS in 197 EOC patients treated between March 2022 and April 2024, with follow-up censored in April 2026. After 1:1 PSM, 80 matched pairs were analyzed. Compared with the PDS group, the NACT+IDS group demonstrated significantly shorter operative time, less blood loss, a higher R0 resection rate, fewer ICU admissions, and a lower incidence of severe complications within 30 days after surgery (all $P < 0.05$). The NACT+IDS group also had higher overall response and disease control rates (both $P < 0.05$), whereas the incidence of grade ≥ 3 chemotherapy-related adverse events was comparable between groups ($P = 0.500$). PFS and OS did not differ significantly between the two cohorts ($P = 0.795$ and $P = 0.062$, respectively), and treatment modality was not independently associated with either endpoint in multivariable Cox regression analyses. Poor tumor differentiation and residual lesion > 1 cm were independently associated with shorter PFS, whereas FIGO stage IV disease, poor tumor differentiation, and residual lesion > 1 cm were independently associated with shorter OS. Subgroup analyses suggested potential differences according to histological subtype; however, these findings were exploratory due to limited sample size. In conclusion, PDS and NACT+IDS offer comparable survival outcomes in patients with advanced EOC, whereas NACT+IDS is associated with improved perioperative safety and higher tumor response rates without increasing severe chemotherapy-related toxicity. Treatment decisions should be individualized according to tumor biology, resectability, and patient characteristics rather than based on a uniform treatment strategy. These findings warrant confirmation in larger prospective studies.

Keywords: Epithelial ovarian cancer, debulking surgery, neoadjuvant chemotherapy, prognostic factors, retrospective cohort study

Introduction

Epithelial ovarian cancer (EOC) remains the most lethal gynecologic malignancy worldwide, with approximately 70% of patients initially diagnosed at advanced stage (FIGO III-IV), largely because of the lack of effective early screening tools and the nonspecific presenting symptoms [1, 2]. Despite aggressive multimodal therapy, the 5-year overall survival (OS) rate for

advanced EOC remains approximately 30%, posing a major challenge in gynecologic oncology [3, 4].

For decades, primary debulking surgery (PDS) followed by platinum-based adjuvant chemotherapy has been the standard treatment for advanced EOC. The fundamental principle of PDS is maximal cytoreduction, with the goal of removing all macroscopically visible lesions at

initial surgery, which has consistently been linked to improved survival [5, 6]. However, PDS is not universally feasible. Extensive intra-abdominal tumor dissemination, involvement of surgically inaccessible sites, and poor patient performance status may preclude complete resection, and suboptimal cytoreduction offers limited survival benefit while exposing patients to substantial perioperative risks and potentially delaying subsequent systemic therapy [7, 8].

To address these limitations, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) has been introduced as an alternative treatment strategy. By administering 2-3 cycles of platinum-based chemotherapy before surgery, NACT can shrink tumor volume, reduce surgical complexity, and increase the likelihood of achieving complete macroscopic resection (R0), a critical determinant of prognosis [9, 10]. Several randomized controlled trials (RCTs) and meta-analyses have demonstrated that NACT+IDS provides OS outcomes comparable to those achieved with PDS while reducing perioperative morbidity and increasing R0 resection rates, establishing it as a valid option for patients unsuitable for immediate surgery [11, 12].

Despite these advances, the optimal initial strategy for advanced EOC remains a subject of intense debate. The recently reported TRUST trial (ENGOT-ov33/AGO-OVAR OP.7), the first phase III RCT conducted exclusively at high-volume centers, reported a significant progression-free survival (PFS) benefit with PDS compared with NACT+IDS, challenging the prevailing view of therapeutic equivalence [12]. Conversely, a large systematic review and meta-analysis of five RCTs (2,380 patients) found no significant difference in OS or PFS between the two approaches, while confirming lower perioperative morbidity and higher R0 resection rates with NACT+IDS [11]. The global real-world SUROVA study similarly reported comparable 5-year OS between the two strategies, whereas a recent 10-year cohort study indicated superior long-term survival with PDS [5, 13]. These conflicting findings may reflect heterogeneity in patient selection, institutional surgical expertise, histological subtypes, and regional clinical practices.

Importantly, evidence specifically derived from Chinese populations remains limited. Popu-

lation-level differences in tumor characteristics, chemotherapy response, and surgical candidacy, findings from international cohorts may not be directly generalizable to Chinese populations. The 2026 Chinese Expert Consensus on Neoadjuvant Chemotherapy for Advanced EOC [14] advocates personalized, patient-centered decision-making rather than a one-size-fits-all approach, underscoring the need for additional region-specific clinical evidence.

Against this background, we conducted a single-center retrospective cohort study using propensity score matching (PSM) to comprehensively compare PDS and NACT+IDS in Chinese EOC patients. Our objectives were threefold: (1) to compare survival outcomes (OS and PFS) between the two strategies; (2) to evaluate differences in surgical safety, tumor response (ORR, DCR, CA125 biochemical response), and chemotherapy-related toxicity; and (3) to identify independent prognostic factors associated with long-term survival, with special attention to the effect of treatment modality after adjustment for key confounders, including molecular biomarkers (BRCA1/2 and homologous recombination deficiency [HRD]) and preoperative indicators of tumor burden. By generating robust evidence from a Chinese population, this study aims to support individualized treatment decisions and address an important knowledge gap in the management of Chinese women with advanced EOC.

Patients and methods

Study design

This retrospective cohort study was conducted at a single medical institution. A total of 197 participants with pathologically confirmed EOC who were admitted to Shandong Provincial Hospital between March 2022 and April 2024 were included. Patients were classified into two groups according to their initial management protocols: a PDS group (n=96), in which patients underwent PDS followed by platinum-based drugs as the core adjuvant chemotherapy regimen; and a NACT+IDS group (n=101), in which patients first received NACT, followed by IDS and postoperative adjuvant chemotherapy. PSM was performed to balance various baseline clinical characteristics between the two groups and reduce potential selection bias. This match adopted a 1:1 nearest-neighbor matching method, with a caliper width of 0.05.

PDS vs NACT+IDS in epithelial ovarian cancer

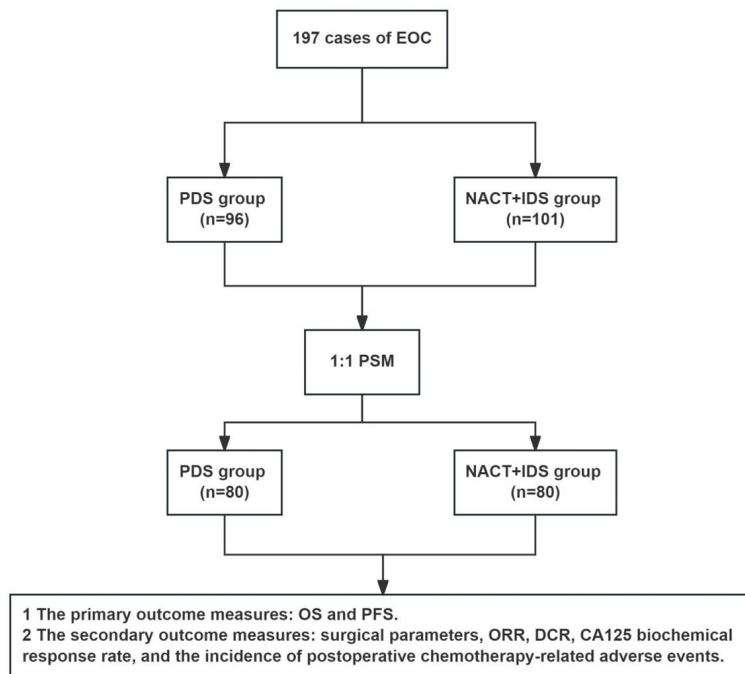


Figure 1. Study flowchart. Note: EOC: epithelial ovarian cancer; PSM: propensity score matching; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery; ORR: overall response rate; DCR: disease control rate; CA125: cancer antigen 125; OS: overall survival; PFS: progression-free survival.

After matching, 80 patients were retained in each group, yielding 80 matched pairs (**Figure 1**).

Inclusion criteria

(1) Pathological confirmation: EOC was histologically confirmed, irrespective of histological subtype. (2) Disease stage: Patients had advanced-stage disease, defined as International Federation of Gynecology and Obstetrics (FIGO) stage III or IV, and were deemed fit for combined surgical debulking plus chemotherapy [15]. (3) Defined therapeutic pathways: Patients received one of the following two standardized treatment sequences: PDS cohort: PDS followed by platinum-based adjuvant chemotherapy. NACT-IDS cohort: NACT followed by IDS and postoperative adjuvant chemotherapy. (4) Admission time and institution: Patients were admitted to and initially diagnosed at Shandong Provincial Hospital between March 2022 and April 2024. (5) Complete clinical records: Complete pathological records, operative notes, chemotherapy records, and follow-up data were available. Follow-up was censored

in April 2026. (6) Assessable clinical outcomes: Data required to evaluate tumor response and survival outcomes were available for statistical analysis.

Exclusion criteria

(1) Non-epithelial ovarian malignancies: Histological findings indicated a non-epithelial ovarian malignancy, including a germ cell tumor, sex cord-stromal tumor, or metastatic tumor originating from another organ. (2) Unconfirmed pathological diagnosis: Adequate histopathological specimens were unavailable for a definite diagnosis, or lesion subtypes could not be categorized as EOC. (3) Previous anti-tumor management: Patients had undergone ovarian cancer-related resection, chemotherapy, radiotherapy, or other anti-cancer interventions before admission to the study center. (4) Concurrent or historical second primary malignancies: Patients presented with a synchronous primary malignancy or a documented history of other malignant tumor that might confound the assessment of survival outcomes [16]. (5) Incomplete standardized treatment: Patients underwent only exploratory laparotomy or tissue biopsy without subsequent PDS or IDS, did not receive postoperative platinum-based adjuvant chemotherapy, or received chemotherapy regimens that did not meet the predefined treatment criteria of this study. (6) Incomplete clinical or follow-up data: Essential pathological or clinical records were unavailable, or follow-up data were insufficient to evaluate OS, PFS, or tumor response. (7) Admission outside the study period: Patients were admitted before March 2022 or after April 2024.

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Data collection and follow-up

Two investigators independently retrieved clinical and pathological data of the 197 patients with EOC who were admitted between March

2022 and April 2024. Medical records were sourced from the hospital's electronic medical record system, pathology database, and imaging archive. The extracted variables included baseline demographic and clinical characteristics, intraoperative parameters, detailed chemotherapy regimens, and treatment response measures. Histological grade was determined according to the fifth edition of the *WHO Classification of Female Genital Tumours* (2020) [17]. Two senior pathologists independently reviewed all hematoxylin & eosin-stained sections while blinded to the patients' clinical data. Tumors were graded based on the proportion of glandular formation and the degree of nuclear atypia: well-differentiated (G1; >95% glandular formation with mild nuclear atypia), moderately differentiated (G2; 50%-95% glandular formation with moderate nuclear atypia), and poorly differentiated (G3; <50% glandular formation with marked nuclear atypia). Disagreements between the two pathologists were resolved by consensus using a multiheaded microscope. Data were independently entered by the two investigators and cross-verification was performed to minimize data-entry errors.

The objective response rate (ORR) throughout chemotherapy was assessed using computed tomography (CT) or magnetic resonance imaging (MRI) in accordance with the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). The serum cancer antigen 125 (CA125) response was evaluated according to the Gynecologic Cancer InterGroup (GCIg) criteria. Adverse reactions induced by chemotherapy were graded according to the Common Terminology Criteria for Adverse Events, version 5.0 (CTCAE 5.0). Follow-up tracking was implemented through a combined strategy of outpatient regular reexaminations and telephone inquiries restricted to overall survival status verification only. Outpatient visits were scheduled every 3 months during the first 2 years after completion of primary treatment and every 6 months thereafter. Follow-up assessments included gynecological examinations, contrast-enhanced imaging, serum tumor marker measurements, and documentation of survival status. The data cutoff date was April 30, 2026. Patients who were lost to follow-up were censored at the date of their last confirmed contact, and survival data were matched and locked accordingly to ensure temporal consistency across the entire cohort.

Chemotherapy regimens

PDS protocol: Adjuvant chemotherapy was initiated 2-4 weeks after primary debulking surgery, provided that wound healing was satisfactory and organ function was adequate for treatment. The regimen consisted of paclitaxel at 175 mg/m² administered as a 3-hour intravenous infusion on day 1, combined with carboplatin at a target area under the concentration-time curve (AUC) of 5-6 administered as a 1-hour intravenous infusion on the same day. Treatment was repeated every 21 days for a total of 6-8 cycles unless disease progression or unacceptable toxicity occurred. Premedication was routinely given 30-60 minutes before paclitaxel infusion to prevent hypersensitivity reactions, including oral dexamethasone 20 mg, intramuscular diphenhydramine 50 mg, and intravenous cimetidine 300 mg. Antiemetic prophylaxis with palonosetron 0.25 mg was administered intravenously prior to each cycle. Dose reductions or treatment delays were permitted according to the severity of hematologic and non-hematologic toxicities per standard guidelines. Recombinant human granulocyte colony-stimulating factor (G-CSF) was used as needed for neutropenia management [18].

NACT+IDS regimen: Patients in the NACT+IDS group received 2-3 cycles of NACT before IDS. The NACT regimen consisted of paclitaxel at 175 mg/m² administered as a 3-hour intravenous infusion plus carboplatin at an AUC of 5-6 administered as a 1-hour intravenous infusion on day 1 of each 21-day cycle. After completion of NACT, tumor response was reassessed. Patients without disease progression who remained eligible for surgery underwent IDS, typically 3-6 weeks after the final NACT cycle.

Following IDS, the remaining adjuvant chemotherapy cycles were completed using the same drugs and dosages, with a planned combined total of 6-8 neoadjuvant and postoperative cycles. Premedication and antiemetic prophylaxis were administered as described for the PDS group. Recombinant human G-CSF was used as needed for primary or secondary prophylaxis of neutropenia. Dose reductions or treatment delays were permitted according to the observed toxicities. Bevacizumab and poly(ADP-ribose) polymerase (PARP) inhibitors were not routinely administered as part of first-

line treatment at our institution during the study period [19].

The number of NACT cycles was determined according to the tumor response after the initial two cycles. Specifically, all patients in the NACT+IDS group initially received two cycles of paclitaxel-carboplatin at 21-day intervals. After the completion of the second cycle, tumor response was evaluated using contrast-enhanced CT/MRI (per RECIST 1.1) and serum CA125 assessment according to the GCIG criteria. Patients who achieved partial response (PR) or complete response (CR) proceeded to IDS. Those with stable disease (SD) received a third cycle of NACT, followed by re-evaluation and subsequent IDS. Patients with progressive disease (PD) after two cycles did not undergo IDS and received alternative management.

Observation indicators

Surgery-related outcomes: Operative duration: Operative time was defined as the interval from the initial skin incision to completion of skin closure and was recorded in minutes (min).

Intraoperative blood loss: Intraoperative blood loss was estimated by combining measurements of fluid collected in suction canisters with the change in the weight of surgical gauze. Total intraoperative blood loss = total fluid volume in the suction canisters - volume of intraoperative irrigation fluid + (weight of blood-soaked gauzes after operation - baseline weight of dry gauzes). The anesthesiologist recorded the suction-canister volume during surgery, while operating room nurses weighed the gauze weights. Estimated blood loss was recorded in milliliters (mL) [20].

Transfusion rate: This transfusion rate was defined as the proportion of patients who received an allogeneic blood transfusions intraoperatively or within the first 24 hours after surgery. The prespecified transfusion criteria included a hemoglobin concentration <80 g/L or acute intraoperative hemorrhage exceeding 20% of the estimated total blood volume. Transfusion data, including cross-matching records, blood transfusion application forms, and administration logs, were retrieved from the hospital information system. The transfusion rate was calculated as the number of patients who received a transfusion relative to the total

number of patients who underwent surgery in each cohort [21].

R0 resection rate: R0 resection was defined as the absence of macroscopically visible residual tumor tissue at the completion of surgery. Attending surgeons made direct judgments of residual lesion status based on intraoperative exploration and documented in the operative report. The R0 resection rate was calculated as the proportion of patients with no macroscopically visible residual disease among all patients who underwent surgery in each group [21].

Postoperative intensive care unit (ICU) admission rate: Postoperative ICU admission was defined as transfer to the ICU for close monitoring or supportive treatment due to hemodynamic instability, respiratory dysfunction, massive hemorrhage, or other severe postoperative complications. Data were obtained from ICU admission records and postoperative progress notes in the electronic medical record system. The ICU stay duration was recorded in hours. The ICU admission rate was calculated as the proportion of patients admitted to the ICU among all patients who underwent surgery in each group [20].

Incidence of severe postoperative complications within 30 days: Postoperative complications occurring within 30 days after surgery were graded according to the Clavien-Dindo classification. Severe postoperative complications were defined as complications of grade III or higher. Two senior gynecologic oncologists independently reviewed postoperative progress records, nursing charts, laboratory results, intervention records, ICU records, and reoperation documentation to assign complication grades. The incidence of severe complications was calculated as the proportion of patients who experienced grade III or higher complications out of all patients who underwent surgery in each group [20].

Chemotherapy efficacy outcomes: ORR was evaluated according to RECIST 1.1. Contrast-enhanced CT or MRI was scheduled every 2-3 adjuvant chemotherapy cycles to measure the longest diameters of target lesions. Two radiologists independently reviewed the images while blinded to the treatment group and clinical outcomes. Therapeutic response was classified as: complete response (CR), partial

response (PR), stable disease (SD), or progressive disease (PD). CR was defined as the disappearance of all target lesions; PR was defined as a decrease of at least 30% in the sum of the diameters of target lesions relative to baseline; PD was defined as an increase of at least 20% in the sum of the diameters of target lesions or the appearance of new lesions; and SD was defined as a response that met neither the criteria for PR nor those for PD. ORR was calculated as the percentage of evaluable patients who attained CR or PR in each group [22].

DCR was also evaluated according to RECIST 1.1 and was defined as the proportion of evaluable patients who achieved CR, PR or SD as their best overall response during postoperative adjuvant chemotherapy. DCR was calculated as the number of patients who achieved CR, PR or SD divided by the total number of patients with an evaluable treatment response in each group [23].

The CA125 biochemical response rate was determined according to the Gynecologic Cancer InterGroup (GCIg) criteria. Serum CA125 levels were measured using a chemiluminescence assay (Roche Diagnostics GmbH, Germany). Peripheral venous blood was drawn before each chemotherapy cycle. A CA125 response was defined as a minimum reduction of 50% from the pretreatment CA125 concentration, confirmed by a subsequent measurement obtained at least 28 days later. The CA125 response rate was calculated as the proportion of patients who met the GCIg response criteria among those eligible for CA125 response evaluation in each group [24, 25].

Chemotherapy safety outcomes: Incidence of grade ≥ 3 chemotherapy-associated adverse events: Chemotherapy-related adverse reactions were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE 5.0). The observation window extended from the first day of the initial chemotherapy cycle to 30 days after completion of the final cycle, encompassing all administered platinum-based chemotherapy (including NACT in the NACT+IDS group and postoperative adjuvant chemotherapy in both groups).

Medical records, laboratory findings (including complete blood counts, liver and kidney func-

tion tests, electrolyte measurements), and documented patient-reported symptoms were reviewed throughout the observation period. The evaluated adverse events included hematologic toxicity, nausea and vomiting, peripheral neuropathy, hepatic and renal impairment, and other clinically relevant toxicities. For each patient, the highest toxicity grade recorded for each adverse event during the observation period was documented. Grade 3 or above events were classified as severe or life-threatening toxicities. The incidence of grade ≥ 3 chemotherapy-related adverse events was calculated as the percentage of patients who experienced any grade ≥ 3 adverse event among all patients who received chemotherapy in each group [26].

Survival outcomes: OS was defined as the interval from histopathological confirmation of EOC to death from any cause and was calculated in months. Multiple follow-up approaches were adopted, including regular outpatient reexaminations, review of inpatient medical records, and telephone interviews. Deaths were verified using hospital mortality records, official death certificates, or confirmation by family members [13]. Subjects who remained alive at the data cutoff date, or who were lost to follow-up were censored at the date on which their survival status was last confirmed.

PFS was defined as the interval from pathological diagnosis of EOC to the first documented disease progression (assessed by contrast-enhanced CT or MRI according to RECIST 1.1 criteria, with imaging evaluation conducted independently by two senior radiologists in a blinded manner) or all-cause death, whichever occurred first, with measurements recorded on a monthly basis. An increase in tumor marker levels, clinical symptoms, or findings from secondary exploratory surgery, in the absence of radiological confirmation, was not considered sufficient evidence of disease progression [13]. Patients who were alive without disease progression were censored at the date of their last evaluable radiological disease assessment.

Preoperative clinical indicators and molecular biomarkers: (1) BRCA1/2 mutation status: Genomic DNA was extracted from peripheral blood samples. Germline BRCA1 and BRCA2 mutations were detected using next-generation sequencing (NGS) on an Illumina platform

(Illumina, San Diego, CA, USA). A custom targeted panel covering all coding exons and exon-intron boundaries (± 20 bp) of *BRCA1* and *BRCA2* was used. Variants were annotated and classified according to the American College of Medical Genetics and Genomics/Association for Molecular Pathology (ACMG/AMP) guidelines.

(2) Homologous recombination deficiency (HRD) status: HRD status was assessed using formalin-fixed, paraffin-embedded (FFPE) tumor specimens and an HRD panel (Amoy Diagnostics Co., Ltd., Xiamen, China). The assay employs a custom hybridization-capture panel targeting approximately 24,000-27,000 single-nucleotide polymorphisms (SNPs) distributed across the genome to assess genomic instability. Sequencing was performed on an Illumina NextSeq500 system using 150-bp paired-end reads. The HRD score, also termed the genomic scar score (GSS), was calculated using the proprietary ADx-GSS algorithm (Amoy Diagnostics), which integrates weighted copy number variations (CNVs) of different types trained on BRCAness events. Patients with a pathogenic *BRCA1/2* mutation and/or a GSS ≥ 50 were defined as HRD-positive.

(3) Maximum tumor diameter: Baseline contrast-enhanced abdominopelvic CT or pelvic MRI obtained before initiation of antitumor treatment were independently reviewed by two senior radiologists. The maximum diameter of the primary ovarian lesion was recorded.

(4) Critical-site involvement: Imaging findings from preoperative CT/MRI were jointly evaluated by radiologists and gynecologic oncologists to determine the presence of tumor involvement at critical anatomical sites, including hepatic hilum, mesenteric root, and diaphragm.

(5) Baseline serum CA125: Venous blood was collected before the initiation of antitumor treatment. Serum CA125 concentrations were measured using a chemiluminescence immunoassay.

(6) Serum albumin: Fasting preoperative venous blood was collected, and serum albumin concentrations were measured using an automatic biochemical analyzer.

Ethical statement

This retrospective study was approved by the Ethics Committee of the Shandong Provincial

Hospital (approval number: 2024-575), and the requirement for informed consent was waived. All procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

Sample size calculation

This was a single-center retrospective cohort study with an exploratory rather than confirmatory design. Therefore, the sample size was not determined using a formal a priori calculation based on a prespecified effect size, but rather by the number of eligible patients who met the inclusion criteria during the recruitment window (March 2022 - April 2024). After 1:1 propensity score matching, 80 patients were retained in each treatment arm, yielding a total of 160 matched patients.

A post-hoc power analysis was conducted for the primary endpoint of OS. Assuming a two-sided significance level of 0.05, an overall event rate of approximately 60% (about 96 events), and a 1:1 allocation ratio, the study had 90% power to detect a hazard ratio (HR) of approximately 0.52 or lower. Thus, the available sample size was sufficient to detect relatively large treatment effects but was underpowered to detect small differences (e.g., HR=0.96) as reported in some meta-analyses [27]. Accordingly, the comparative and prognostic analyses should be interpreted as exploratory and hypothesis-generating, and their findings require confirmation in larger prospective studies.

Statistical analyses

All data sorting and statistical analyses were performed using SPSS 26.0 software (IBM Corp., NY, USA). To mitigate potential selection bias, 1:1 PSM (caliper 0.05) was first employed to reduce baseline imbalances between the treatment groups. Propensity scores were estimated using age, body mass index (BMI), FIGO stage, histological type, comorbidities, histological grade, Eastern Cooperative Oncology Group performance status (ECOG PS), and ascites. Variables reflecting tumor biology and treatment selection, including maximum tumor diameter, critical-site involvement, baseline CA125 level, serum albumin concentration, *BRCA1/2* mutation status, and HRD status, exhibited substantial between-group differences and limited common support and were

therefore not included in the matching model. These variables were instead considered as covariates in the subsequent multivariate Cox regression analyses. PSM-matched covariate balance was evaluated using standardized mean difference (SMD), with an SMD<0.2 considered indicative of acceptable balance.

Normally distributed continuous variables are presented as mean $\pm$ standard deviation (SD), and were compared using the independent-sample t-test. Non-normally distributed continuous data are expressed as median (interquartile range), and were compared using the Mann-Whitney U test. Categorical variables were presented as numbers and percentages, and were compared using the chi-square test or Fisher's exact test, as appropriate.

OS was defined as the interval from histopathological confirmation of EOC to all-cause death or the last valid follow-up visit. PFS was defined as the interval from histopathological confirmation of EOC to the first documented disease progression or all-cause death, whichever occurred first. Survival curves were estimated using the Kaplan-Meier method, and compared using the log-rank test.

Univariable Cox proportional hazards regression analyses were initially performed to evaluate factors associated with OS and PFS. Variables with a *P* value <0.10 in univariate screening were incorporated into the multivariable Cox proportional hazards regression models to identify independent prognostic factors for OS and PFS. The variables considered included age, FIGO stage, histological grade, histological subtype, ECOG PS, ascites, treatment modality, residual disease, BRCA1/2 mutation status, HRD status, maximum tumor diameter, critical-site involvement, baseline CA125 concentration, and serum albumin concentration. Results are reported as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). All tests were two-sided, and *P*<0.05 was considered statistically significant.

Results

Baseline clinical data

Table 1 summarizes the baseline clinical characteristics of patients with advanced EOC in the two treatment groups before and after

PSM. Prior to matching, no significant differences were observed between the PDS group and the NACT+IDS group in age, BMI, concurrent chronic illnesses (hypertension, diabetes mellitus, cardiovascular disorders), histological subtypes, histological grade, FIGO stage, ECOG PS, or abdominal ascites (all *P*>0.05). However, SMD for several variables exceeded 0.2, indicating potentially meaningful baseline imbalances despite the absence of statistically significant differences.

After 1:1 PSM, no significant differences were observed in the matched variables between the two cohorts, including age, BMI, FIGO disease stage, tumor histology, coexisting systemic diseases, histological grade, ECOG PS and ascites (all *P*>0.05), and the corresponding absolute SMDs were <0.2. According to the prespecified balance criterion, the two matched cohorts achieved acceptable balance in these baseline characteristics and were included in subsequent comparative analyses.

Preoperative clinical indicators and molecular biomarkers

Table 2 summarizes intergroup comparisons of baseline clinical parameters and molecular biomarkers between the matched PDS and NACT+IDS cohort. No statistically significant intergroup differences were observed in the distribution of *BRCA1/2* mutation (*P*=0.719) or mean HRD scores (*P*=0.652), with small effect sizes detected for both molecular markers.

In contrast, significant intergroup differences were observed in tumor burden and nutritional indicators. Compared with the PDS group, the NACT+IDS group demonstrated a larger maximum tumor diameter (*P*<0.001), higher baseline serum CA125 levels (*P*<0.001), a higher prevalence of critical-site involvement (45.0% vs. 26.3%, *P*=0.013), and lower preoperative serum albumin concentrations (*P*<0.001).

Surgical outcomes

Operative time was significantly shorter in the NACT+IDS cohort than in the PDS group (185.55 $\pm$ 52.26 vs. 246.75 $\pm$ 68.53 min; *P*<0.001, Cohen's *D*=1.004, 95% CI: 42.16-80.24 min). Intraoperative blood loss was also markedly lower in the NACT+IDS group (285.35 $\pm$ 120.57 vs. 512.65 $\pm$ 201.73 mL, *P*<0.001, Co-

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Table 1. Comparison of baseline characteristics between the two groups before and after PSM

Indicators	Before PSM					After PSM				
	PDS group (n=96)	NACT+IDS group (n=101)	P	t/ χ^2	SMD	PDS group (n=80)	NACT+IDS group (n=80)	P	t/ χ^2	SMD
Age (years, mean $\pm$ SD)	62.00 $\pm$ 12.44	63.16 $\pm$ 12.46	0.515	-0.653	-0.12	62.83 $\pm$ 11.54	62.88 $\pm$ 11.93	0.979	-0.027	-0.01
BMI (kg/m ² , mean $\pm$ SD)	22.56 $\pm$ 3.64	22.74 $\pm$ 3.41	0.713	-0.369	-0.07	22.67 $\pm$ 3.69	22.74 $\pm$ 3.57	0.901	-0.124	-0.02
FIGO staging			0.242	1.366	-0.24			1.000	<0.001	<0.001
III	62 (64.6)	57 (56.4)				47 (58.8)	47 (58.8)			
IV	34 (35.4)	44 (43.6)				33 (41.2)	33 (41.2)			
Histological type [n (%)]			0.512	2.301	-0.18			0.879	0.677	-0.07
High-grade serous carcinoma	61 (63.5)	58 (57.4)				48 (60.0)	46 (57.4)			
Endometrioid carcinoma	12 (12.5)	16 (15.8)				10 (12.4)	13 (16.3)			
Clear cell carcinoma	8 (8.3)	14 (13.9)				11 (13.8)	9 (11.3)			
Mucinous carcinoma	15 (15.6)	13 (12.8)				11 (13.8)	12 (15.0)			
Combined with hypertension [n (%)]	31 (32.3)	35 (34.7)	0.726	0.123	0.07	25 (31.3)	28 (35.0)	0.614	0.254	0.11
Combined with diabetes [n (%)]	19 (19.8)	23 (22.8)	0.610	0.261	0.10	15 (18.8)	17 (21.3)	0.693	0.156	0.09
Combined with cardiovascular disease [n (%)]	15 (15.6)	19 (18.8)	0.554	0.350	0.12	11 (13.8)	14 (17.5)	0.514	0.427	0.15
Histological grade [n (%)]			0.425	1.711	-0.15			0.803	0.438	-0.05
Well-differentiated	18 (18.7)	15 (14.9)				14 (17.4)	13 (16.3)			
Moderately differentiated	24 (25.0)	20 (19.8)				21 (26.3)	18 (22.5)			
Poorly differentiated	54 (56.3)	66 (65.3)				45 (56.3)	49 (61.2)			
ECOG PS [n (%)]			0.107	4.463	-0.32			0.635	0.909	-0.14
0	42 (43.8)	33 (32.7)				35 (43.8)	31 (38.7)			
1	44 (45.8)	48 (47.5)				35 (43.8)	35 (43.8)			
2	10 (10.4)	20 (19.8)				10 (12.4)	14 (17.5)			
Presence of ascites [n (%)]	64 (66.7)	75 (74.3)	0.243	1.365	0.24	51 (63.8)	56 (70.0)	0.401	0.705	0.19

Notes: PSM: propensity score matching; SMD: standardized mean difference; SD: standard deviation; BMI: body mass index; FIGO: international federation of gynecology and obstetrics; ECOG PS: Eastern cooperative oncology group performance status; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

PDS vs NACT+IDS in epithelial ovarian cancer

Table 2. Comparison of preoperative clinical indicators and molecular biomarkers between the two groups after PSM

Indicators	PDS group (n=80)	NACT+IDS group (n=80)	P	Effect size (Cohen's D/Phi)	t/ χ^2	95% CI of the difference
BRCA1/2 mutation status [n (%)]						
Mutant	20 (25.0)	22 (27.5)	0.719	-0.028	0.129	-
Wild-type	60 (75.0)	58 (72.5)				
HRD (scores, mean $\pm$ SD)	54.51 $\pm$ 14.48	55.55 $\pm$ 14.56	0.652	-0.071	-0.452	-5.57, 3.50
Maximum tumor diameter (cm, mean $\pm$ SD)	5.35 $\pm$ 2.03	8.55 $\pm$ 2.05	<0.001	-1.571	-9.935	-3.84, -2.56
Critical site involvement (hepatic hilum/mesenteric root/diaphragm) [n (%)]	21 (26.3)	36 (45.0)	0.013	-0.196	6.132	-
Baseline CA125 (U/mL, mean $\pm$ SD)	1192.21 $\pm$ 630.43	2650.50 $\pm$ 850.49	<0.001	-1.948	-12.320	-1692.22, -1224.36
Serum albumin (g/L, mean $\pm$ SD)	38.24 $\pm$ 4.05	33.35 $\pm$ 5.05	<0.001	1.070	6.767	3.47, 6.33

Notes: PSM: propensity score matching; 95% CI: 95% confidence interval; BRCA: breast cancer gene; HRD: homologous recombination deficiency; CA125: cancer antigen 125; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

Table 3. Comparison of surgery-related parameters between the two groups after PSM

Indicators	PDS group (n=80)	NACT+IDS group (n=80)	P	Effect size (Cohen's D/Phi)	t/ χ^2	95% CI of the difference
Operation time (min, mean $\pm$ SD)	246.75 $\pm$ 68.53	185.55 $\pm$ 52.26	<0.001	1.004	6.352	42.16, 80.24
Intraoperative blood loss (mL, mean $\pm$ SD)	512.65 $\pm$ 201.73	285.35 $\pm$ 120.57	<0.001	1.368	8.651	175.31, 279.29
R0 resection rate [n (%)]	55 (68.8)	66 (82.5)	0.043	-0.160	4.103	-
Postoperative ICU admission rate [n (%)]	18 (22.5)	7 (8.8)	0.017	0.189	5.736	-
Incidence of severe complications within 30 days after operation [n (%)]	20 (25.0)	9 (11.3)	0.024	0.178	5.096	-

Notes: PSM: propensity score matching; 95% CI: 95% confidence interval; ICU: intensive care unit; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

Table 4. Comparison of treatment response between the two groups

Indicators	PDS group (n=80)	NACT+IDS group (n=80)	<i>P</i>	Effect size (Phi)	χ^2
ORR [n (%)]	42 (52.5)	55 (68.8)	0.035	-0.166	4.425
DCR [n (%)]	63 (78.8)	73 (91.3)	0.027	-0.175	4.902
Biochemical response rate of CA125 [n (%)]	63 (78.8)	68 (85.0)	0.305	-0.081	1.053

Notes: ORR: overall response rate; DCR: disease control rate; CA125: cancer antigen 125; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

hen's $D=1.368$, 95% CI: 175.31-279.29 mL). Both outcomes demonstrated large effect sizes.

The R0 resection rate was significantly higher in the NACT+IDS group than in the PDS group (82.5% vs. 68.8%, $P=0.043$, $\Phi=-0.160$). Moreover, the NACT+IDS group also had a lower postoperative ICU admission rate (8.8% vs. 22.5%, $P=0.017$, $\Phi=0.189$) and a lower incidence of severe postoperative adverse events (11.3% vs. 25.0%, $P=0.024$, $\Phi=0.178$). The detailed data are summarized in **Table 3**.

Therapeutic response

As shown in **Table 4**, the ORR was significantly higher in the NACT+IDS group than in the PDS group (68.8% vs. 52.5%, $P=0.035$, $\Phi=-0.166$). Similarly, the DCR was significantly higher in the NACT +IDS group (91.3% vs. 78.8%, $P=0.027$, $\Phi=-0.175$). However, no significant difference was observed in the CA125 biochemical response rate between the two arms (85.0% vs. 78.8%, $P=0.305$, $\Phi=-0.081$).

Chemotherapy-related adverse events

No statistically significant intergroup differences were observed between the PDS cohort and NACT+IDS cohort in the incidence of individual grade ≥ 3 chemotherapy-related adverse events, including myelosuppression (10.0% vs. 7.5%, $P=0.576$), chemotherapy-induced nausea and vomiting (7.5% vs. 5.0%, $P=0.514$), peripheral neurotoxicity (5.0% vs. 7.5%, $P=0.514$), hepatotoxicity (2.5% vs. 2.5%, $P=1.000$), hypersensitive reactions (2.5% vs. 2.5%, $P=1.000$), diarrhea (2.5% vs. 2.5%, $P=1.000$), or fatigue (5.0% vs. 2.5%, $P=0.405$). The overall incidence of grade ≥ 3 chemotherapy-related adverse events were comparable between the two groups (35.0% vs. 30.0%, $P=0.500$), as detailed in **Table 5**.

PFS

The median PFS was 15.06 months (95% CI: 13.07-17.05 months) in the PDS group and 15.12 months (95% CI: 13.44-16.80 months) in the NACT+IDS group. The Kaplan-Meier PFS survival curves were similar, and the log-rank test showed no significant differences between the two groups ($P=0.795$; **Figure 2**).

OS

The median OS was 30.58 months (95% CI: 27.75-33.41 months) in the PDS group and 26.26 months (95% CI: 22.79-29.73 months) in the NACT+IDS group. The Kaplan-Meier OS curve for the PDS cohort was generally above that for the NACT+IDS group; however, the log-rank test showed no statistically significant intergroup difference ($P=0.062$; **Figure 3**). Although the median OS was approximately 4.3 months longer in the PDS group, this difference did not reach statistical significance.

Factors associated with PFS in Cox proportional hazards regression model

Variables with a P -value <0.10 in the univariable analyses were entered into the multivariable Cox proportional hazards regression model for PFS (**Tables 6** and **S1**). After adjustment, poor tumor differentiation was independently associated with shortened PFS compared with well-to-moderately differentiated tumors ($HR=1.819$, 95% CI: 1.161-2.849, $P=0.009$). Residual disease >1 cm after surgery was also independently associated with shorter PFS compared with R0 resection ($HR=1.413$, 95% CI: 1.053-1.897, $P=0.021$).

In contrast, no significant associations with PFS were observed for FIGO stage IV disease ($HR=1.207$, 95% CI: 0.829-1.758, $P=0.327$), high-grade serous histological type ($HR=0.525$, 95% CI: 0.010-28.772, $P=0.753$), ECOG PS 2

Table 5. Comparison of the incidence of chemotherapy-related adverse events between the two groups

Indicators	PDS group (n=80)	NACT+IDS group (n=80)	P	Effect size (Phi)	χ^2
Myelosuppression [n (%)]					
Grade ≥ 3	8 (10.0)	6 (7.5)	0.576	0.044	0.313
Nausea and vomiting [n (%)]					
Grade ≥ 3	6 (7.5)	4 (5.0)	0.514	0.052	0.427
Peripheral neurotoxicity [n (%)]					
Grade ≥ 3	4 (5.0)	6 (7.5)	0.514	-0.052	0.427
Liver function impairment [n (%)]					
Grade ≥ 3	2 (2.5)	2 (2.5)	1.000	<0.001	<0.001
Allergic reaction [n (%)]					
Grade ≥ 3	2 (2.5)	2 (2.5)	1.000	<0.001	<0.001
Diarrhea [n (%)]					
Grade ≥ 3	2 (2.5)	2 (2.5)	1.000	<0.001	<0.001
Fatigue [n (%)]					
Grade ≥ 3	4 (5.0)	2 (2.5)	0.405	0.066	0.693
Overall grade ≥ 3 [n (%)]	28 (35.0)	24 (30.0)	0.500	0.053	0.456

Notes: PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery. P values are uncorrected for multiple comparisons and are presented for descriptive purposes only; no formal multiplicity adjustment was applied given the exploratory nature of the safety analysis.

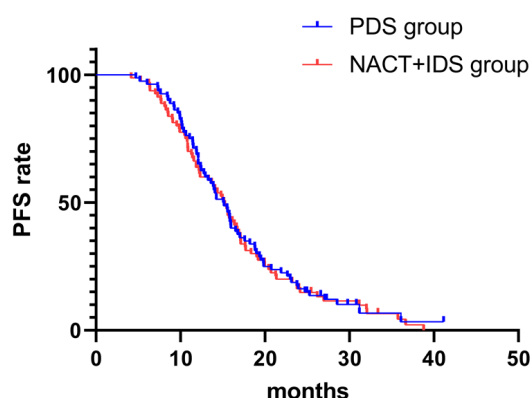


Figure 2. Comparison of PFS between the two groups. The x-axis is extended to 60 months for graphical consistency, yet the actual maximum follow-up duration was approximately 48-50 months. The decline of the survival curve toward zero at the tail solely reflects data censoring due to insufficient follow-up time and the exhaustion of at-risk subjects, rather than a true 5-year survival rate of zero. Therefore, the present follow-up duration is inadequate to yield a reliable estimate of 5-year survival. Notes: PFS: progression free survival; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

(HR=4.190, 95% CI: 0.075-238.521, P=0.486), ascites (HR=0.892, 95% CI: 0.466-1.706, P=0.730), residual disease ≤ 1 cm (HR=1.071,

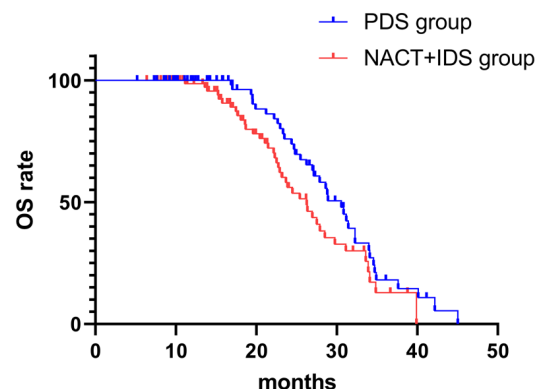


Figure 3. Comparison of OS between the two groups. The x-axis is extended to 60 months for graphical consistency, yet the actual maximum follow-up duration is approximately 48-50 months. The decline of the survival curve toward zero at the tail solely reflects data censoring due to insufficient follow-up time and the exhaustion of at-risk subjects, rather than a true 5-year survival rate of zero. Therefore, the present follow-up duration is inadequate to yield a reliable estimate of 5-year survival. Notes: OS: overall survival; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

95% CI: 0.644-1.781, P=0.791), BRCA1/2 wild-type status (HR=1.853, 95% CI: 0.375-9.157, P=0.449), or critical-site involvement (HR=

Table 6. Cox proportional hazards regression model for screening independent prognostic factors affecting PFS

Indicators	B	P	HR	95% CI for HR
FIGO staging (Reference: Stage III)				
Stage IV	0.188	0.327	1.207	0.829, 1.758
Histological grade (Reference: Well-to-moderately differentiated)				
Poorly differentiated	0.598	0.009	1.819	1.161, 2.849
Histological type (Reference: Non-serous type)				
High-grade serous carcinoma	-0.644	0.753	0.525	0.010, 28.772
ECOG PS (Reference: Score 0-1)				
Score 2	1.433	0.486	4.190	0.075, 238.521
Ascites (Reference: Absent)				
Present	-0.114	0.730	0.892	0.466, 1.706
Residual disease after surgery (Reference: R0)				
≤1 cm	0.069	0.791	1.071	0.644, 1.781
>1 cm	0.346	0.021	1.413	1.053, 1.897
BRCA1/2 mutation status (Reference: Mutant)				
Wild-type	0.617	0.449	1.853	0.375, 9.157
Critical site involvement (Reference: Absent))				
Present	-0.158	0.648	0.854	0.433, 1.682

Notes: FIGO: International Federation of Gynecology and Obstetrics; ECOG PS: Eastern Cooperative Oncology Group performance status.

0.854, 95% CI: 0.433-1.682, $P=0.648$). Treatment strategy was not significantly associated with PFS after adjustment for confounders.

Factors associated with OS in Cox proportional hazards regression model

Variables with a P -value <0.10 in the univariable analyses were entered into the multivariable Cox proportional hazards regression model for OS (**Tables 7** and **S2**). After adjustment, advanced FIGO stage IV disease was independently associated with a significantly higher risk of death compared with stage III disease ($HR=2.359$, 95% CI: 1.287-4.324, $P=0.006$). Poor tumor differentiation was also independently associated with shorter OS compared with well-to-moderately differentiated lesions ($HR=2.460$, 95% CI: 1.393-4.345, $P=0.002$). Residual disease >1 cm after surgery also independently associated with shorter OS compared with R0 resection ($HR=2.096$, 95% CI: 1.176-3.737, $P=0.012$).

In contrast, no significant associations with OS were observed for residual disease ≤ 1 cm ($HR=1.589$, 95% CI: 0.881-2.864, $P=0.124$), *BRCA1/2* wild-type status ($HR=0.700$, 95% CI: 0.355-1.381, $P=0.304$), or critical-site involve-

ment ($HR=0.982$, 95% CI: 0.529-1.823, $P=0.954$).

PFS and OS in patients with high-grade serous carcinoma

Figure 4 presents the Kaplan-Meier curves for PFS and OS according to initial treatment strategy among patients with high-grade serous carcinoma. The median PFS was 15.77 months (95% CI: 13.48-18.06 months) in the PDS group and 11.40 months (95% CI: 10.30-12.50 months) in the NACT+IDS group. Although the Kaplan-Meier curve for the PDS group was generally above that for the NACT+IDS group, the difference between groups did not reach statistical significance ($P=0.248$). The median OS was 28.89 months (95% CI: 23.42-34.36 months) in the PDS group and 26.95 months (95% CI: 22.17-31.73 months) in the NACT+IDS group. Similarly, no statistically significant difference in OS was observed between the two treatment groups ($P=0.470$).

Comparison of PFS and OS in patients with non-high-grade serous carcinoma

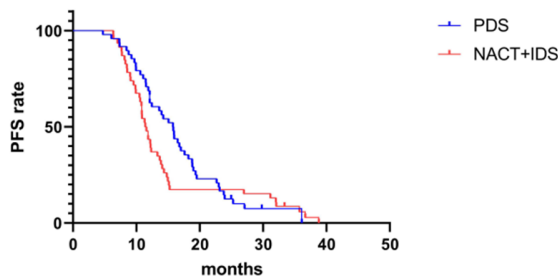
The dual-panel Kaplan-Meier curves in **Figure 5** present PFS (left) and OS (right) among

Table 7. Cox proportional hazards regression model for screening independent prognostic factors affecting OS

Indicators	B	P	HR	95% CI for HR
FIGO staging (Reference: Stage III)				
Stage IV	0.858	0.006	2.359	1.287, 4.324
Histological grade (Reference: Well-to-moderately differentiated)				
Poorly differentiated	0.900	0.002	2.460	1.393, 4.345
Residual disease after surgery (Reference: R0)				
≤1 cm	0.463	0.124	1.589	0.881, 2.864
>1 cm	0.740	0.012	2.096	1.176, 3.737
BRCA1/2 mutation status (Reference: Mutant)				
Wild-type	-0.357	0.304	0.700	0.355, 1.381
Critical site involvement (Reference: Absent)				
Present	-0.018	0.954	0.982	0.529, 1.823

Notes: FIGO, International Federation of Gynecology and Obstetrics.

PFS of high-grade serous carcinoma group



OS of high-grade serous carcinoma group

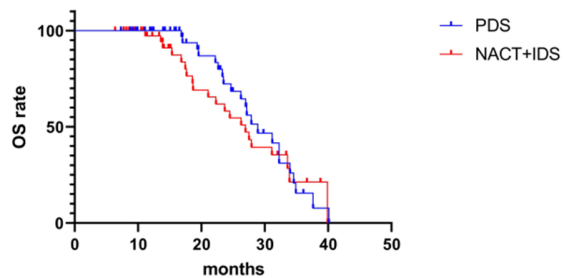
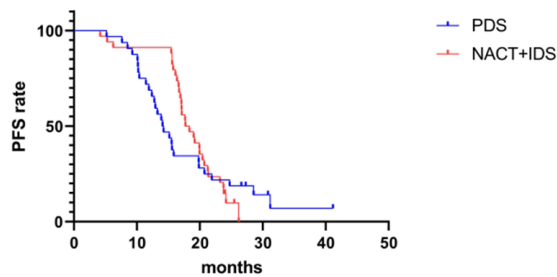


Figure 4. Comparison of PFS and OS in patients with high-grade serous carcinoma. Notes: PFS: progression free survival; OS: overall survival; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

PFS of non-high-grade serous carcinoma group



os of non-high-grade serous carcinoma

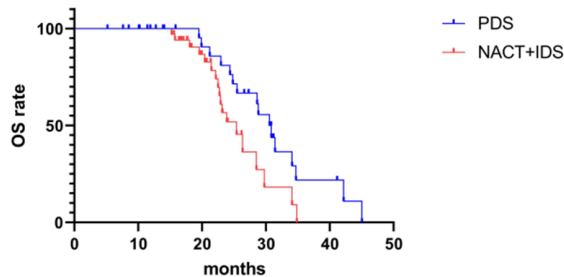


Figure 5. Comparison of PFS and OS in patients with non-high-grade serous carcinoma. Notes: PFS: progression free survival; OS: overall survival; PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy; IDS: interval debulking surgery.

patients with non-high-grade serous carcinoma, stratified according to treatment strategy. The median PFS was 14.06 months (95% CI: 11.44-16.68 months) in the PDS group and 17.72 months (95% CI: 15.03-20.41 months)

in the NACT+IDS group. Although the Kaplan-Meier curve for the NACT+IDS group remained higher than the curve for PDS group during most of the follow-up period, the between-group difference in PFS was not statistically sig-

nificant ($P=0.586$). The median OS was 30.58 months (95% CI: 26.77-34.39 months) in the PDS group and 25.41 months (95% CI: 22.07-28.76 months) in the NACT+IDS group. The curve for the PDS group was generally above that for the NACT+IDS group, and the between-group difference was statistically significant ($P=0.030$), indicating that PDS was associated with longer OS in this subgroup.

Discussion

After PSM, this retrospective study compared survival outcomes, tumor response, perioperative outcomes, and chemotherapy-related safety between EOC patients treated with PDS and those treated with NACT+IDS. No statistically significant differences in OS or PFS were observed between the two cohorts. The NACT+IDS group demonstrated superior surgical outcomes, including a shorter operative duration, less blood loss, a higher R0 resection rate, and a lower incidence of severe postoperative complications. The incidence of grade ≥ 3 chemotherapy-related adverse events did not differ significantly between groups. Multivariable regression analyses indicated that treatment modality was not an independent prognostic factor for PFS or OS, whereas tumor differentiation, FIGO stage, and the extent of residual lesion were associated with survival outcomes. These findings should be interpreted cautiously because of the exploratory study design and the absence of formal model validation.

The comparable survival outcomes suggest that surgical timing may not be the sole determinant of outcomes in advanced EOC. Although surgery was delayed in the NACT+IDS group, its higher R0 resection rate (82.5% vs. 68.8%) may have contributed to observed similarity in survival outcomes [11, 28, 29]. The improved surgical safety profiles associated with NACT+IDS, including a shorter operative time, less blood loss, fewer ICU admissions, and fewer severe complications, may partly reflect the reduction in tumor burden and surgical complexity achieved with neoadjuvant treatment [30]. Importantly, comparable grade ≥ 3 chemotherapy-related toxicity between groups indicates that addition of NACT did not increase systemic toxicity in this cohort [31].

Compared with previous studies, this study has several unique features. First, evidence specifi-

cally derived from Chinese EOC patients remain limited, and this study provides additional real-world data from a Chinese clinical setting. Population-level differences in tumor characteristics, healthcare delivery, surgical candidacy, and treatment patterns may influence the applicability of findings from international cohorts to Chinese clinical practice. Second, our Cox regression analyses considered molecular biomarkers (BRCA1/2, HRD) and preoperative indicators of tumor burden (maximum tumor diameter, critical site involvement, baseline CA125, serum albumin). This approach allowed these clinically relevant factors to be considered when evaluating associations between treatment strategy and survival. Third, exploratory analyses stratified by histological subtype revealed that PDS was associated with longer OS compared with NACT+IDS among patients with non-high-grade serous carcinoma ($P=0.030$), whereas no such difference was observed among patients with high-grade serous carcinoma. This subtype-specific finding has not been previously reported in the Chinese EOC population.

Broadly consistent with published meta-analyses [11, 27] and the SUROVA real-world study [13], our findings reported no substantial differences in survival between the two strategies. However, our PFS findings differ from those of the TRUST trial, which reported a PFS advantage with PDS at high-volume centers with specialized surgical expertise [12]. Differences in patient selection, baseline tumor burden, and institutional treatment practices may partly explain these divergent findings. The inconsistent findings of other retrospective studies [5, 32] underscore the importance of patient selection, institutional proficiency, and tumor characteristics when interpreting comparative outcomes between PDS and NACT+IDS.

Postoperative residual tumor >1 cm was confirmed as an independent risk factor for shorter PFS and OS, consistent with findings from previous large cohort studies [33, 34]. Poor tumor differentiation was also associated with shorter PFS and OS, whereas FIGO stage IV disease was associated with shorter OS. These associations may reflect the more aggressive biological behavior of advanced and poorly differentiated tumors. Importantly, after adjustment for tumor burden, FIGO stage, and histological dif-

ferentiation, treatment modality was not independently associated with either survival outcome, suggesting that prognosis is more strongly driven by inherent tumor biology than by treatment sequence. Given the absence of independent validation, this interpretation remains preliminary.

Our findings have several clinical implications. For patients with a high tumor burden, critical-site involvement, poor performance status, or a low probability of achieving complete macroscopic resection with upfront surgery, NACT+IDS may represent a safe alternative that does not compromise long-term survival while offering improved surgical safety and higher response rates. Treatment selection should incorporate tumor characteristics, resectability, surgical risk, performance status, and patient preferences rather than applying a uniform strategy. In particular, among non-high-grade serous carcinoma patients, PDS may confer superior OS if optimal cytoreduction is achievable; conversely, for patients unlikely to achieve R0 upfront, NACT+IDS can increase complete resection rates without sacrificing survival. Third, residual disease >1 cm should be rigorously monitored as a surgical quality metric regardless of treatment strategy. Fourth, comparable chemotherapy toxicity profiles support the feasibility of NACT without substantially increasing adverse events.

Comparison with previous studies further places our findings in context. Previous meta-analyses and RCTs have primarily evaluated overall study population, with limited exploration of histological subtype-specific effects. Our study report a potential OS disadvantage of NACT+IDS specifically in Chinese patients with non-high-grade serous carcinoma, providing guidance to avoid NACT overuse in this subgroup. Additionally, although the SUROVA Asian subgroup analysis suggested that Chinese patients might derive greater benefit from NACT, our overall population did not show this trend - possibly due to differences in patient composition, NACT cycles, or maintenance therapy. Thus, the SUROVA subgroup findings should not be directly generalized to all Chinese EOC patients without further local validation.

In summary, our findings provide Chinese population-based evidence supporting individualized initial treatment selection within a multi-

disciplinary framework, integrating tumor burden, histological subtype, molecular biomarkers, resectability, and performance status. Given the single-center retrospective design, residual confounding, exploratory subgroup analyses, and lack of model validation, these conclusions should be interpreted as exploratory and hypothesis-generating, requiring confirmation in larger prospective studies.

Limitations and directions for subsequent research

Several limitations of this study should be acknowledged. First, this was a single-center retrospective study with a modest sample size (80 matched patients per group) and a maximum follow-up duration of approximately 48-50 months. These factors limited the statistical power to detect modest survival differences and precluded reliable estimation of 5-year survival. Second, although PSM was used to balance the demographic and routine clinical characteristics, and multivariable adjustment was subsequently performed to control for additional measured confounders, PSM did not eliminate the intergroup differences in the tumor burden and clinical indicators listed in **Table 2**, including maximum tumor diameter, baseline CA125 concentration, critical-site involvement, and serum albumin concentration. These variables were controlled only through covariate adjustment in the Cox regression models. Consequently, residual confounding related to measured or imperfectly measured tumor characteristics, as well as unmeasured factors such as surgeon expertise, perioperative nutritional support, and institutional treatment-selection practices, cannot be excluded. Third, Data on maintenance therapy with PARP inhibitors or bevacizumab and treatments administered after recurrence were not systematically captured. In particular, secondary cytoreductive surgery or subsequent lines of therapy may have influenced OS estimates. In addition, the Cox regression models were not formally assessed for the proportional hazards assumption (Schoenfeld residuals) or C-index calculation. Neither internal validation, such as bootstrap validation, nor external validation was performed. The modest events-per-variable ratio may have resulted in overfitting and unstable estimates. Consequently, the identified prognostic factors and treatment

comparisons should be interpreted as exploratory and hypothesis-generating rather than confirmatory. The subgroup analyses stratified by histological subtype (HGSC vs. non-HGSC) were purely descriptive without formal interaction testing. The relatively small subgroup sizes (approximately 94 and 66 patients, respectively) limited to determine whether histological subtype modified the association between treatment strategy and survival.

Future prospective, multi-center studies should include larger sample sizes, longer follow-up, systematic collection of maintenance and post-recurrence treatment data, formal model validation, and patient-reported outcomes and quality-of-life measures. Further studies are also needed to determine the optimal number of NACT cycles and identify patients most likely to benefit from PDS or NACT+IDS.

Conclusions

The results of this analysis suggest that the long-term survival outcomes of patients may not be determined solely by the selection of the initial treatment regimen. In comparison, the degree of tumor differentiation, the pathological staging of FIGO surgery, and the size of residual lesions after surgery emerged as potential independent influencing factors affecting patients' long-term prognosis within this study sample. However, because the Cox regression models were not internally or externally validated, these findings should be viewed as exploratory and require confirmation in future prospective studies with larger sample sizes.

Disclosure of conflict of interest

None.

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PDS vs NACT+IDS in epithelial ovarian cancer

Table S1. Univariate Cox regression for PFS

Variable	HR	95% CI	P
FIGO IV (vs. III)	0.717	0.518, 0.992	0.045
Poorly differentiated (vs. well/moderate)	1.684	1.196, 2.371	0.003
HGSC (vs. non-serous)	0.611	0.436, 0.854	0.004
ECOG PS 2 (vs. 0-1)	0.599	0.428, 0.838	0.003
Ascites present (vs. absent)	0.731	0.516, 1.036	0.078
NACT+IDS (vs. PDS)	1.044	0.756, 1.440	0.795
Residual ≤1 cm (vs. R0)	0.731	0.452, 1.183	0.202
Residual >1 cm (vs. R0)	0.409	0.204, 0.818	0.011
BRCA1/2 wild-type (vs. mutant)	0.003	0.001, 0.015	<0.001
HRD (per 1-unit increase)	1.002	0.990, 1.014	0.760
Maximum tumor diameter (per cm)	0.972	0.915, 1.032	0.349
Critical site involvement (present)	0.056	0.031, 0.101	<0.001
Baseline CA125 (per U/mL)	1.000	1.00, 1.00	0.309
Serum albumin (per g/L)	0.996	0.966, 1.027	0.799

Table S2. Univariate Cox regression for OS

Variable	HR	95% CI	P
FIGO IV (vs. III)	1.770	1.110, 2.825	0.017
Poorly differentiated (vs. well/moderate)	1.770	1.022, 3.068	0.042
HGSC (vs. non-serous)	1.066	0.671, 1.695	0.786
ECOG PS 2 (vs. 0-1)	1.085	0.682, 1.729	0.729
Ascites present (vs. absent)	1.057	0.666, 1.675	0.816
NACT+IDS (vs. PDS)	1.240	0.784, 1.959	0.358
Residual ≤1 cm (vs. R0)	0.626	0.355, 1.106	0.107
Residual >1 cm (vs. R0)	0.354	0.113, 0.973	0.044
BRCA1/2 wild-type (vs. mutant)	0.322	0.192, 0.539	<0.001
HRD (per 1-unit increase)	0.993	0.974, 1.013	0.511
Maximum tumor diameter (per cm)	1.058	0.965, 1.159	0.230
Critical site involvement (present)	0.375	0.229, 0.614	<0.001
Baseline CA125 (per U/mL)	1.000	1.00, 1.00	0.359
Serum albumin (per g/L)	0.990	0.948, 1.034	0.657