Risk Factors for Recurrence and Complications Following Cytoreductive Surgery in Platinum-Resistant Ovarian Cancer: A Retrospective Cohort Study

Ann. Ital. Chir., 2026 97, 3: 560–570
https://doi.org/10.62713/aic.4351

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AIM: This study aims to identify independent risk factors for tumor recurrence and postoperative complications in platinum-resistant ovarian cancer patients undergoing cytoreductive surgery.

METHODS: This study retrospectively included 96 patients with platinum-resistant ovarian cancer who underwent cytoreductive surgery between January 2020 and December 2022. Of these, 76 patients were in the recurrence group, and 20 patients were in the non-recurrence group. Among them, 84 patients developed postoperative complications and 12 did not. Recurrence was defined as disease progression evidenced by radiological findings according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, or tumor recurrence confirmed by histopathology. Complications within 30 days were graded using the Clavien–Dindo system (grade $\geq$II). Collected clinicopathological variables included surgical duration, peritoneal cancer index (PCI), surgical complexity score (SCS), and postoperative cancer antigen 125 (CA125), the latter measured after two cycles of adjuvant chemotherapy to assess recurrence. Variables with $p < 0.05$ in univariate analysis were included in a multivariate logistic regression model to identify independent risk factors. Receiver operating characteristic (ROC) curve analysis was used to assess the discriminative power of the identified predictors.

RESULTS: Recurrence was significantly associated with longer surgical duration, elevated postoperative CA125, increased PCI, fewer chemotherapy cycles, and suboptimal cytoreductive surgery (all $p < 0.05$). Multivariate analysis identified surgical duration (odds ratio (OR) = 2.076), postoperative CA125 (OR = 1.193), and PCI (OR = 1.247) as independent risk factors for recurrence. Exploratory ROC analysis suggested moderate discriminative ability of the combined factors (area under the curve (AUC): 0.84), although no model validation was performed. Surgical duration, CA125, and PCI each demonstrated moderate predictive values, with AUCs of 0.77, 0.66, and 0.67, respectively. Complications were independently associated with elevated postoperative CA125; however, the complication model demonstrated only modest discriminative ability (AUC = 0.71). These results should be interpreted as exploratory.

CONCLUSIONS: Prolonged surgical duration, elevated postoperative CA125 levels, and higher PCI scores were independently associated with recurrence in patients with platinum-resistant ovarian cancer, while elevated postoperative CA125 levels were also associated with postoperative complications. These factors demonstrated moderate discriminative ability and may serve as potential markers for postoperative risk stratification. However, these findings are exploratory in nature and require external validation.

Keywords: ovarian cancer; platinum-resistant ovarian cancer; cancer antigen 125; recurrence; postoperative complications

Introduction

Ovarian cancer remains one of the most lethal gynecologic malignancies worldwide, with a high mortality rate despite advances in cytoreductive surgery and platinum-based chemotherapy [1–3]. Recurrence occurs in the majority of patients, and among these, platinum-resistant ovarian cancer (PROC)—defined as recurrence within six months after completion of platinum-based treatment [4,5]—represents the most aggressive subset, with limited treatment options and poor survival outcomes [6–8].

Submitted: 16 September 2025 Revised: 23 November 2025 Accepted: 9 December 2025 Published: 10 March 2026
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Editor: Roberto Cirocchi

In selected PROC patients, cytoreductive surgery remains an important component of disease management, as the completeness of resection continues to be a key determinant of prognosis [9–11]. Surgical outcomes and postoperative complications in this setting are influenced by multiple perioperative factors, including tumor burden, ascites, and surgical duration; however, reliable predictors are still lacking [12,13]. Identifying such predictors is crucial given the high-risk nature of PROC and the substantial morbidity associated with extensive surgical procedures.

Serum cancer antigen 125 (CA125) is widely recognized as a biomarker for disease monitoring and treatment response in ovarian cancer [14–16]. However, its postoperative prognostic value—particularly in PROC patients who have already demonstrated resistance to platinum-based therapy—remains insufficiently defined. Prior studies primarily focused on advanced or recurrent ovarian cancer populations without specifically addressing platinum-

resistant disease [17,18], leaving uncertainty regarding the role of postoperative CA125 in risk stratification for PROC.

Given these gaps, a comprehensive evaluation integrating postoperative CA125 with detailed perioperative factors—such as the peritoneal cancer index (PCI), surgical duration, and intraoperative blood loss—may provide more accurate insight into recurrence risk and postoperative complications in this underrepresented patient group. Such combined perioperative assessments remain limited in current literature despite their potential to guide individualized surgical and postoperative management.

Therefore, this study aimed to investigate the association between postoperative CA125 levels and perioperative clinical variables with both recurrence and postoperative complications in patients with PROC. Clarifying these associations may generate hypotheses for future prospective studies on individualized postoperative assessment and follow-up.

Methods

Study Design and Setting

This retrospective cohort study was conducted by reviewing the medical records of patients treated at Jiangxi Maternal and Child Health Hospital from January 2020 to December 2022. All patients were treated and followed in the gynecological oncology ward, with follow-up conducted via outpatient visits and telephone contact. The study was approved by the Ethics Committee of Jiangxi Maternal and Child Health Hospital (No. EC-KY-2024137) and conducted in adherence to the Declaration of Helsinki.

Patient Selection

One hundred and forty-two consecutive patients with newly diagnosed primary epithelial ovarian cancer undergoing cytoreductive surgery were initially screened and identified from the hospital database between January 2020 and December 2022. Of the identified patients, 31 were excluded due to incomplete perioperative data, 10 had non-epithelial histology, and 5 were lost to follow-up within 6 months, leaving 96 eligible patients included in the final analysis. None of the patients received neoadjuvant chemotherapy. The detailed inclusion process is illustrated in Fig. 1. Disease recurrence during follow-up was determined according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and/or histopathological confirmation [19]. Based on follow-up outcomes, 76 patients met the diagnostic criteria for PROC and were classified into the recurrence group, while the remaining 20 patients without recurrence within this interval comprised the non-recurrence group.

Postoperative complications within 30 days were graded according to the Clavien–Dindo classification (grade $\geq$II) [20], and the classification process revealed 84 patients with complications and 12 without complications. Patients were followed longitudinally after surgery to capture recurrence and postoperative outcomes. Platinum-resistant ovarian cancer was defined as recurrence occurring within six months after completion of platinum-based chemotherapy [21,22]. At each follow-up visit, serum CA125 levels were measured using routine institutional procedures, and imaging was performed when clinically indicated. CA125 testing was only used as an adjunctive measure when radiologic or clinical suspicion of recurrence was present.

Inclusion and Exclusion Criteria

Inclusion criteria included: (1) histopathologically confirmed ovarian cancer; (2) availability of postoperative follow-up data sufficient to determine platinum response status (platinum-resistant or non-resistant); and (3) age $>$18 years. Patients who met the criteria for cytoreductive surgery underwent screening. Exclusion criteria applied during the initial screening included: (1) incomplete perioperative or follow-up data; (2) non-epithelial ovarian histology; and (3) loss to follow-up before assessment of platinum response status.

Data Collection

The current cohort primarily comprised patients with extensive tumor burden and high surgical complexity, since our center is a tertiary gynecologic oncology referral hospital. This is reflected by the relatively high median PCI and high surgical complexity score (SCS) scores observed in the cohort, as well as the frequent need for multi-organ cytoreductive procedures, including bowel resection and diaphragmatic surgery. Such case-mix characteristics inherently increase both recurrence risk and postoperative morbidity, and therefore, the event rates in this study should be interpreted in the context of a highly selected, high-risk surgical population. The final sample size was limited by the relatively low incidence of PROC during the study period, strict eligibility criteria, and the requirement for complete perioperative and follow-up data. Intestinal surgery was defined as intestinal resection and/or stoma formation during cytoreductive surgery. PCI was scored intraoperatively according to the established 13-region system (score range 0–39). Surgical complexity was evaluated using the SCS which assigns weighted points based on the extent of procedures performed. Collected variables included demographics (age, body mass index [BMI], educational level, marital status), clinical/pathological features (history of abdominal surgery, chemotherapy cycles, differentiation grade, histological type, International Federation of Gynecology and Obstetrics [FIGO] stage, CA125 after two postoperative chemotherapy cycles), and surgical indicators (ascites volume, surgical duration, intraoperative blood loss, transfusion volume, residual disease status and surgical outcomes). Postoperative complications within 30 days were graded as Clavien–Dindo $\geq$II and were identified from prespecified clinical documentation, laboratory results, imaging reports, and if available findings of positive microbiological cultures documented in the electronic medical record.

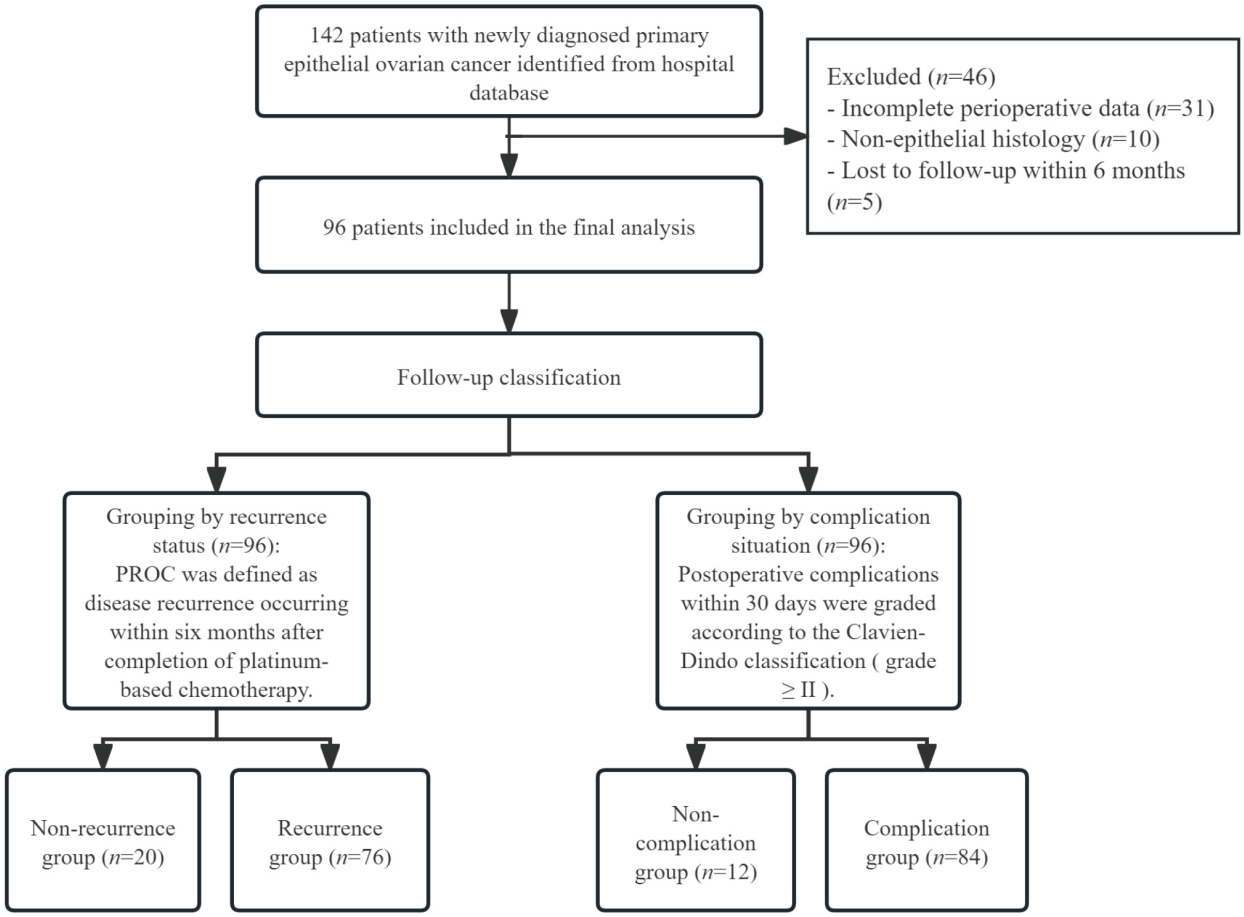

Fig. 1. STROBE flow diagram of patient screening and cohort formation. This diagram shows the overall screening process and the formation of the final study cohort, indicating the number of excluded cases and the reasons for exclusion, followed by classification of included patients into the recurrence and non-recurrence groups, as well as the complication and non-complication groups. Abbreviations: STROBE, strengthening the reporting of observational studies in epidemiology; PROC, platinum-resistant ovarian cancer.

Preoperative tumor burden was assessed using computed tomography/magnetic resonance imaging (CT/MRI) and confirmed intraoperatively, with PCI scored as per Jónsdóttir *et al.* [23]. Surgical complexity was quantified using the SCS [24]. The SCS was assessed according to the system proposed by Aletti *et al.* [24], which assigns weighted points based on the extent of cytoreductive surgery (peritoneal stripping, bowel resection, diaphragmatic surgery, splenectomy, etc.) to quantify overall surgical effort. Bowel surgery was defined as intestinal resection and/or stoma formation performed during the index cytoreductive procedure and was recorded as a measure of surgical complexity. Histology was categorized as "serous", "mucinous" and "other" (endometrioid, clear cell, mucinous, low-grade serous, mixed), given the predominance of high-grade serous carcinoma in advanced disease.

Postoperative CA-125 levels were measured after two cycles of adjuvant chemotherapy, a time point selected to predict survival in patients with advanced epithelial ovarian cancer [25,26].

Statistical Analysis

Statistical analysis was performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was employed to assess the normality of continuous variables. Normally distributed data were expressed as mean ± standard deviation (SD) and compared using the *t*-test. Non-normally distributed data were expressed as median (P25, P75) and analyzed using the rank-sum test. Categorical variables were presented as frequency and percentage, and compared using the chi-square or Fisher's exact test. Multicollinearity among key predictors (residual disease, PCI, surgical duration) was examined using variance inflation factors (VIF; all <5). Variables with $p < 0.05$ in univariate analysis were entered into a multivariate logistic regression model (Enter method). Due to class imbalance (76 vs 20), results were interpreted with caution, and 95% confidence intervals were reported. The primary aim of the analysis was to identify independent risk factors using multivariate logistic regression. Receiver operating characteristic (ROC) curve and area under the curve (AUC) analyses were used to exploratoryly evaluate the discriminative performance of identified predictors.

Results

Baseline Characteristics of Platinum-Resistant Ovarian Cancer Patients

Table 1 summarizes the baseline demographic and clinicopathological characteristics of the platinum-resistant cohort.

Table 1. Baseline information of patients.

Characteristic	Patients (n = 96)
Age (years)	53.78 ± 7.86
BMI (kg/m^2)	22.79 ± 2.34
Educational level	
Primary school or below	29 (30.21%)
Secondary school	50 (52.08%)
University or above	17 (17.71%)
Marital status	
Married	91 (94.79%)
Unmarried	5 (5.21%)
Recurrence (yes/no)	76/20
Postoperative complications (yes/no)	84/12
History of abdominal surgery	
Yes	37 (38.54%)
No	59 (61.46%)
Chemotherapy cycles	
≤5 cycles	63 (65.63%)
>5 cycles	33 (34.38%)
Differentiation grade	
Moderate/high	45 (46.88%)
Low	51 (53.12%)
Histological type	
Serous	53 (55.21%)
Mucinous	25 (26.04%)
Others	18 (18.75%)
FIGO stage	
III	44 (45.83%)
IV	52 (54.17%)
Ascites volume (mL)	465 (275.00, 780.00)
Surgical duration (hours)	4.56 ± 1.27
Intraoperative blood loss (mL)	600 (400.00, 800.00)
Transfusion volume (mL)	700 (500.00, 900.00)
Surgical outcome	
Residual tumor <1 cm	70 (72.92%)
Residual tumor ≥1 cm	26 (27.08%)
Postoperative CA125 (U/mL)	26.61 (24.09, 29.98)
Bowel surgery	
No	64 (66.67%)
Anastomosis	24 (25.00%)
Stoma formation	8 (8.33%)
PCI (score)	22 (20.00, 25.00)
SCS (score)	5 (4.00, 5.00)

Abbreviations: BMI, body mass index; CA125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics; PCI, peritoneal cancer index; SCS, surgical complexity score.

Analysis of Factors Influencing Recurrence in PROC Patients

Of the 96 patients reviewed, 76 were classified into the recurrence group and 20 into the non-recurrence group based on documented progression during follow-up. Compared with the non-recurrence group, patients with recurrence had significantly longer surgical duration, higher postoperative CA125 levels and PCI scores, a lower rate of optimal cytoreductive surgery, and received fewer chemotherapy cycles (all $p < 0.05$). No significant differences were found in other clinical or surgical factors between the groups (Table 2).

Logistic Multivariate Analysis of Risk Factors for PROC Recurrence

In the final multivariable logistic regression model, surgical duration (odds ratio (OR) = 2.076; 95% CI, 1.154–3.738; p = 0.015), postoperative CA125 (OR = 1.193; 95% CI, 1.006–1.415; p = 0.042) and PCI (OR = 1.247; 95% CI, 1.003–1.551; p = 0.047) emerged as independent predictors of recurrence among patients with PROC (Table 3). Other variables, including chemotherapy cycle number and surgical outcome, did not reach statistical significance and were therefore excluded from the final model.

Diagnostic Performance of Indicators for Predicting PROC Recurrence

Receiver operating characteristic analysis showed that the combined model demonstrated modest discriminative ability for recurrence risk and should be regarded as exploratory (AUC = 0.84, sensitivity = 73.68%, specificity = 85.00%, Youden's index = 0.59). Surgery duration also demonstrated good discriminative ability (AUC = 0.77, sensitivity = 67.11%, specificity = 80.00%). Postoperative CA125 (AUC = 0.66, sensitivity = 59.21%, specificity = 75.00%) and PCI (AUC = 0.67, sensitivity = 85.53%, specificity = 40.00%) had moderate predictive value (Table 4, Fig. 2). These findings suggest an association with recurrence risk, rather than establishing their definitive predictive capacity.

Analysis of Factors Influencing Complications in PROC Patients

Among the 96 patients, 84 were classified into the complication group and 12 into the non-complication group based on documented progression during follow-up. The high incidence reflects the inclusion of heavily pretreated, platinum-resistant cases undergoing extensive cytoreductive procedures, including bowel resection and anastomosis, which are inherently associated with increased morbidity. Patients with postoperative complications had significantly longer surgical duration, higher postoperative CA125 levels, and higher PCI scores compared to those without complications (all $p < 0.05$). Other clinical or surgical factors showed no significant differences between the groups (Table 5).

Table 2. Univariate analysis of factors influencing recurrence in PROC patients.

Factor	Recurrence group (n = 76)	Non-recurrence group (n = 20)	t/χ^2/z	p-value
Age (years)	53.76 ± 7.94	53.85 ± 7.76	0.044	0.965
BMI (kg/m^2)	22.75 ± 2.38	22.96 ± 2.23	0.357	0.722
Educational level				
Primary school or below	23 (30.26%)	6 (30.00%)		
Secondary school	37 (48.69%)	13 (65.00%)	3.114	0.211
University or above	16 (21.05%)	1 (5.00%)		
Marital status				
Married	74 (97.37%)	17 (85.00%)	—	0.059
Unmarried	2 (2.63%)	3 (15.00%)		
History of abdominal surgery				
Yes	29 (38.16%)	8 (40.00%)	0.023	0.880
No	47 (61.84%)	12 (60.00%)		
Chemotherapy cycles				
≤5	54 (71.10%)	9 (45.00%)	4.764	0.029
>5	22 (28.90%)	11 (55.00%)		
Differentiation grade				
Moderate/high	36 (47.40%)	9 (45.00%)	0.036	0.850
Low	40 (52.60%)	11 (55.00%)		
Histological type				
Mucinous	20 (26.32%)	5 (25.00%)		
Serous	44 (57.89%)	9 (45.00%)	2.193	0.334
Others	12 (15.79%)	6 (30.00%)		
FIGO stage				
III	36 (47.40%)	8 (40.00%)	0.346	0.620
IV	40 (52.60%)	12 (60.00%)		
Ascites volume (mL)	465 (262.50, 770.00)	460 (327.50, 817.50)	0.735	0.462
Surgical duration (hours)	4.67 ± 1.26	3.84 ± 1.11	2.064	<0.001
Intraoperative blood loss (mL)	600 (400.00, 800.00)	400 (325.00, 875.00)	1.007	0.314
Transfusion volume (mL)	700 (500.00, 900.00)	500 (350.00, 975.00)	0.975	0.329
Surgical outcome				
Satisfactory tumor reduction (residual tumor <1 cm)	59 (77.60%)	11 (55.00%)	4.107	0.043
Unsatisfactory tumor reduction (residual tumor ≥1 cm)	17 (22.40%)	9 (45.00%)		
Postoperative CA125 (U/mL)	27.83 ± 4.39	25.55 ± 2.84	5.031	0.030
Bowel surgery				
None	48 (63.13%)	16 (80.00%)		
Anastomosis	20 (26.32%)	4 (20.00%)	—	0.263
Stoma formation	8 (10.53%)	0 (0.00%)		
PCI (score)	22.00 (20.00, 26.00)	21.00 (18.25, 23.00)	−2.362	0.018
SCS (score)	4.00 (4.00, 5.00)	4.50 (4.00, 5.00)	−0.210	0.834

Abbreviation: PROC, platinum-resistant ovarian cancer. —, indicates that Fisher's exact test was applied, therefore there is no χ^2 value.

Table 3. Final multivariate logistic regression analysis for recurrence within six months.

Factor	β	SE	Wald χ^2 value	p-value	OR (95% CI)
Chemotherapy cycle number	−0.806	0.623	1.676	0.195	0.447 (0.132–1.513)
Surgical outcome	−0.678	0.632	1.149	0.284	0.508 (0.147–1.754)
Surgical duration (hours)	0.731	0.300	5.935	0.015	2.076 (1.154–3.738)
Postoperative CA125 (U/mL)	0.177	0.087	4.137	0.042	1.193 (1.006–1.415)
PCI (score)	0.221	0.111	3.934	0.047	1.247 (1.003–1.551)

Note: only variables retained in the final multivariate model are shown. Abbreviation: OR, odds ratio.

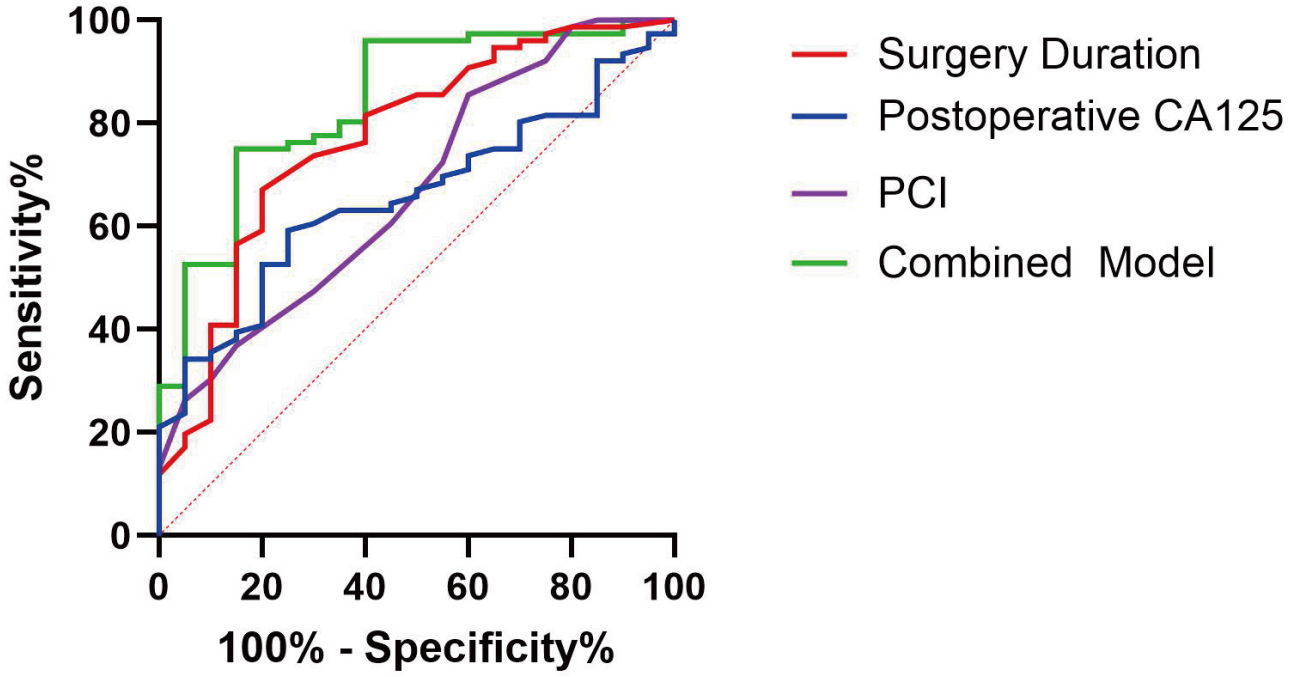

Fig. 2. ROC curves comparing the diagnostic performance of surgical duration, postoperative CA125, PCI, and the combined model in recurrence prediction. Abbreviations: PCI, peritoneal cancer index; CA125, cancer antigen 125; ROC, receiver operating characteristic.

Table 4. Predictive performance of surgical and biological indicators for recurrence in PROC.

Factor	AUC	SE	Sensitivity %	Specificity %	Youden's index
Surgical duration (hours)	0.77	0.06	67.11%	80.00%	0.47
Postoperative CA125 (U/mL)	0.66	0.06	59.21%	75.00%	0.34
PCI (score)	0.67	0.07	85.53%	40.00%	0.26
Combined model	0.84	0.05	73.68%	85.00%	0.59

Abbreviation: AUC, area under the curve.

Multivariate Logistic Regression Analysis of Factors Influencing Postoperative Complications in PROC Patients

Multivariate logistic regression analysis confirmed postoperative CA125 as the only independent risk factor for complications in PROC patients (OR = 1.278, 95% CI: 1.025–1.593, $p = 0.029$). Neither surgical duration (OR = 1.654, 95% CI: 0.912–2.999, $p = 0.097$) nor PCI score (OR = 1.235, 95% CI: 0.956–1.594, $p = 0.107$) achieved statistical significance (Table 6).

Diagnostic Value of Postoperative CA125 for Predicting Postoperative Complications in PROC Patients

ROC curve analysis indicated that postoperative CA125 was associated with the occurrence of postoperative complications. The model demonstrated modest discriminative ability (AUC = 0.71; sensitivity = 91.67%, specificity = 53.57%), indicating limited utility as a standalone predictor (Table 7, Fig. 3).

Discussion

Ovarian cancer remains the most lethal gynecological malignancy, with a 5-year survival rate below 50% [2]. Type II epithelial ovarian cancers, predominantly high-grade serous carcinoma (about 75%), are aggressive—frequently diagnosed during advanced stages—and associated with *P53* and *BRCA* mutations [27]. Standard management for ovarian cancer involves cytoreductive surgery, chemotherapy, and maintenance therapy [28,29]. Phosphoinositide 3-kinase (PI3K) pathway activation contributes to chemoresistance and genomic stability, and its inhibition can increase chromosomal instability via aurora kinase B [30]. Complete cytoreductive surgery provides the most favorable prognosis [31], followed by residual disease $\leq$1 cm at a single anatomical site [9]; however, residual tumors $<$1 cm in multiple sites have been associated with increased odds of platinum resistance [10]. Chemoresistance persists as a major therapeutic barrier [32]. Emerging proteomic technologies aid in elucidating tumor adaptation mechanisms and developing novel therapeutic strategies [33]. Identifying recurrence risk factors in PROC is thus crucial for guiding individualized management and improving outcomes.

Table 5. Analysis of factors influencing postoperative complications in PROC patients.

Factor	Complication group (n = 84)	Non-complication group (n = 12)	t/χ^2/z	p-value
Age (years)	53.92 ± 7.80	52.83 ± 8.57	0.445	0.658
BMI (kg/m^2)	22.63 ± 2.36	23.93 ± 1.92	1.811	0.073
Educational level				
Primary school or below	28 (33.33%)	1 (8.33%)		
Secondary school	43 (51.19%)	7 (58.34%)	4.166	0.125
University or above	13 (15.48%)	4 (33.33%)		
Marital status				
Married	80 (95.24%)	11 (91.67%)	—	0.495
Unmarried	4 (4.76%)	1 (8.33%)		
History of abdominal surgery				
Yes	32 (61.90%)	5 (41.70%)	0.057	0.812
No	29 (38.10%)	7 (58.30%)		
Chemotherapy cycles				
≤5	55 (65.50%)	8 (66.70%)	0.007	0.935
>5	29 (34.50%)	4 (33.30%)		
Differentiation grade				
Moderate/high	38 (45.20%)	7 (58.30%)	0.723	0.395
Low	46 (54.80%)	5 (41.70%)		
Histological type				
Mucinous	21 (25.00%)	4 (33.33%)		
Serous	48 (57.14%)	5 (41.67%)	1.021	0.533
Others	15 (17.86%)	3 (25.00%)		
FIGO stage				
III	40 (47.60%)	4 (33.30%)	0.863	0.353
IV	44 (52.40%)	8 (66.70%)		
Ascites volume (mL)	470 (310.00, 780.00)	220 (102.50, 865.00)	1.396	0.163
Surgical duration (hours)	4.81 ± 1.18	3.64 ± 1.19	2.145	0.035
Intraoperative blood loss (mL)	500 (400.00, 875.00)	600 (350.00, 700.00)	0.479	0.632
Transfusion volume (mL)	600 (350.00,700.00)	700 (375.00, 800.00)	0.507	0.612
Surgical outcome				
Satisfactory tumor reduction (residual tumor <1 cm)	62 (73.80%)	11 (66.70%)	0.271	0.602
Unsatisfactory tumor reduction (residual tumor ≥1 cm)	17 (26.20%)	9 (33.30%)		
Postoperative CA125 (U/mL)	27.79 ± 4.31	24.79 ± 2.20	6.039	0.023
Bowel surgery				
None	55 (65.48%)	9 (75.00%)		
Anastomosis	22 (26.19%)	2 (16.67%)	—	0.885
Stoma formation	7 (8.33%)	1 (8.33%)		
PCI (score)	22 (20.00, 25.75)	22 (20.00, 21.75)	−2.188	0.029
SCS (score)	4 (4.00, 5.00)	4 (4.00, 5.00)	−1.521	0.128

—, indicates that Fisher's exact test was applied, therefore there is no χ^2 value.

Table 6. Final multivariate logistic regression analysis for postoperative complications in PROC patients.

Factor	β	SE	Wald χ^2 value	p-value	OR (95% CI)
Surgical duration (hours)	0.503	0.304	2.749	0.097	1.654 (0.912–2.999)
Postoperative CA125 (U/mL)	0.245	0.113	4.748	0.029	1.278 (1.025–1.593)
PCI (score)	0.211	0.131	2.605	0.107	1.235 (0.956–1.594)

Note: only the independent predictors retained in the final multivariate model are shown.

Our logistic regression analyses identified prolonged surgical duration and elevated postoperative CA125 levels as variables associated with higher odds of recurrence in PROC patients, but these findings should be regarded as exploratory, given the limited sample size and retrospective design. Accordingly, the results should not be directly

Table 7. Diagnostic performance of postoperative CA125 for predicting postoperative complications in PROC patients.

Factor	AUC	SE	Sensitivity %	Specificity %	Youden's index
Postoperative CA125 (U/mL)	0.71	0.06	91.67%	53.57%	0.45

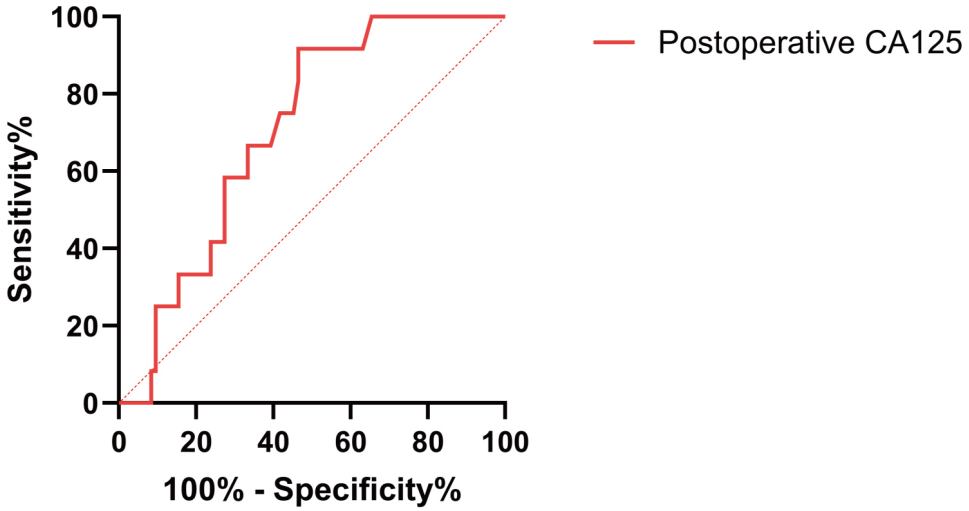

Fig. 3. ROC curve illustrating the diagnostic performance of postoperative CA125 for predicting complications in PROC patients.

extrapolated to clinical decision-making without prospective validation. Unlike previous study that primarily examined overall ovarian cancer populations or recurrence alone, our work specifically targeted PROC and simultaneously assessed both surgical and biochemical indicators [34]. The correlation between surgical duration and complications approached but did not reach statistical significance, potentially due to a small sample size or other confounding factors. Prolonged surgical duration may reflect greater tumor burden or technical complexity, leading to increased intraoperative trauma. Additionally, extended surgical duration is also associated with higher intraoperative blood loss and a higher likelihood of postoperative infection [35,36], potentially indirectly promoting tumor growth or metastasis. Therefore, prolonged surgical duration may reflect greater tumor burden or technical complexity and could be explored in future studies as a factor associated with recurrence, while maintaining the goal of optimal cytoreduction. In this cohort, longer surgical duration was associated with higher odds of recurrence; however, this association should be interpreted cautiously and viewed as exploratory rather than as evidence of a definitive clinical threshold. However, the AUC values observed in our study represent only moderate discriminative ability. Therefore, these indicators should be interpreted as being associated with recurrence rather than robust predictive markers. External validation and calibration in larger multicenter cohorts are warranted.

Our analyses further demonstrated PCI as an independent predictor of recurrence in PROC. Specifically, for each one-point increase in PCI, the odds of recurrence increased by 24.7%. In contrast, PCI did not remain an independent predictor of postoperative complications after adjustment for other variables, which may reflect the limited statistical power of the study and the potential confounding influence of CA125 and surgical duration. Patients with elevated PCI exhibited higher odds of recurrence, even after adjusting for surgical duration and postoperative CA125. This aligns with recent meta-analyses and cohort studies showing that a high PCI is associated with poorer survival outcomes. For instance, one review reported a pooled hazard ratio of 2.79 for overall survival and 1.89 for progression-free survival in patients with elevated PCI [37]. Additionally, intraoperative PCI thresholds have been reported to be associated with incomplete cytoreductive surgery and worse recurrence-free survival [38]. These findings may provide exploratory insight into the potential role of PCI in surgical planning and postoperative risk assessment, rather than indicating direct clinical applicability. Although residual disease status is a well-established prognostic factor, it was not independently associated with recurrence in our multivariate model. VIF analysis did not indicate problematic multicollinearity; rather, the observed attenuation likely reflects both the limited variability in residual disease and overlapping prognostic information with PCI and surgical duration, which directly capture tumor burden and surgical complexity. Therefore, our results should not be interpreted as diminishing the importance of optimal cytoreductive surgery in broader settings.

In the present study, most patients achieved optimal cytoreduction, which resulted in limited variation in residual disease status. This likely explains why surgical outcome was not identified as an independent predictor of recurrence in our multivariate analysis, despite its well-established prognostic significance in residual disease.

CA125, as a widely used marker for postoperative monitoring in ovarian cancer patients, has been associated with recurrence and treatment response in previous study [39]. In our cohort, elevated postoperative CA125 was statistically associated with higher odds of recurrence (AUC = 0.66), although the absolute difference between groups was small and the discriminative ability remained moderate. CA125 dynamics may reflect underlying disease activity associated with recurrence risk; however, their clinical implications for follow-up strategies should be cautiously interpreted [40]. Elevated postoperative CA125 levels may reflect higher tumor burden; however, given the small absolute differences observed, this finding should be interpreted with caution. Regular postoperative monitoring of CA125 may provide clinically informative insights; however, the impact of CA125 on prognosis or clinical decision-making in PROC has not yet been established and requires further study. In the present study, the combined use of surgical indicators and postoperative CA125 showed modest discriminative ability for recurrence and should be regarded as exploratory.

Postoperative CA125 was also the only independent predictor of postoperative complications (OR = 1.278, AUC = 0.71). Elevated CA125 may reflect not only tumor activity but also systemic inflammatory responses or perioperative stress, and is associated with a higher likelihood of postoperative complications, including infection, bleeding, or bowel dysfunction. This duality may help explain why postoperative CA125 elevation does not necessarily imply residual tumor activity. Patients with elevated postoperative CA125 were associated with higher odds of postoperative complications; however, the implications of this association for postoperative monitoring strategies remain uncertain. However, early postoperative CA125 interpretation requires caution due to non-specific elevation from inflammation and peritoneal handling. Thus, changes in CA125 levels, rather than isolated values, should be interpreted in the context of overall clinical findings.

Univariate analysis showed that patients who received fewer chemotherapy cycles ($\leq$5) were more likely to relapse. However, this finding is likely explained by confounding factors such as disease burden, postoperative recovery, and treatment tolerance, rather than a true causal relationship. Patients with more advanced disease or poorer performance status typically receive more cycles of chemotherapy, which may bias the apparent association. Therefore, the observed relationship should be interpreted cautiously and should not be regarded as evidence of a beneficial effect of fewer chemotherapy cycles on clinical outcomes.

The median interval between surgery and chemotherapy was 24 days (interquartile range 18–32), aligning with the recommended timelines (3–5 weeks) for optimal outcomes [41]. Delays due to postoperative complications prolong this interval [42]. Although our dataset lacked standardized complication grading, post-hoc review suggests such delays may be associated with tumor progression—a limitation necessitating prospective investigation.

The notably high recurrence (76/96) and complication rates (84/96) should be interpreted in the context of this highly selected, high-risk population. Most patients presented with extensive disease burden, and many required complex multi-organ cytoreduction, which naturally results in elevated postoperative morbidity in referral-center settings. This retrospective cohort design enabled efficient analysis of real-world data but carries inherent limitations. Given the limited sample size and the severe class imbalance in both recurrence (76 vs 20) and complication outcomes (84 vs 12), the multivariate logistic regression models are subject to a low events-per-variable ratio. This increases the likelihood of unstable regression coefficients, wide confidence intervals, and potential overfitting. As such, the multivariate analysis results should be interpreted cautiously and considered exploratory rather than definitive. Taken together, the small sample size and pronounced class imbalance substantially limit the strength of inference, and all findings should therefore be interpreted with particular caution. Importantly, no internal or external validation was performed in this study; therefore, all model-related findings should be regarded as exploratory. Possible selection and information bias may result from reliance on medical records, and unmeasured confounders could affect the interpretation of observed associations. The single-center setting restricts generalizability. The imbalance between recurrence and non-recurrence groups (76 vs 20) may have reduced statistical power and model stability; bias-reduced methods such as Firth's regression should be considered in future studies. The sample size was limited by the low incidence of PROC and strict inclusion criteria. The timing of postoperative CA125 measurement—after two chemotherapy cycles—likely contributed to the relatively low, narrowly distributed values and may conflate surgical and chemotherapeutic effects, introducing potential time-dependent bias. Although postoperative CA125 was statistically associated with recurrence, the absolute difference between groups (~2 U/mL) was modest and may lack clinical significance. Additionally, standardized diagnostic criteria for complications and consistent follow-up intervals were not uniformly applied, introducing potential information and monitoring bias. The type of primary treatment (primary debulking surgery versus neoadjuvant chemotherapy) can influence surgical complexity and outcomes [43,44], but all patients in the present study underwent primary debulking surgery, which minimized heterogeneities in surgical complexity and outcomes. Model performance was moderate (AUC = 0.71) and unvalidated; therefore, future multicenter studies with larger cohorts and standardized methodologies are warranted.

Conclusions

Prolonged surgery, elevated postoperative CA125, and high PCI are independently associated with recurrence in

platinum-resistant ovarian cancer in this exploratory cohort. Elevated CA125 is also correlated with complications. These associations should be considered exploratory, and further investigation and external validation of the potential factors are warranted before consideration for postoperative stratification or clinical decision-making.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

LW and ZX substantially contributed to the conception or design of the work. LY and JW contributed to the acquisition, analysis, or interpretation of data for the work. LW and ZX drafted the manuscript. All authors have been involved in revising the manuscript critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study received approval from the Ethics Committee of Jiangxi Maternal and Child Health Hospital (No. EC-KY-2024137) and adhered to the Declaration of Helsinki. Informed consent was waived because all clinical data were anonymized and de-identified prior to analysis, and no identifiable information was collected.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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