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Post-Neoadjuvant Chemotherapy Cancer Antigen-125 Levels and their association with Progression-Free and Overall Survival in Advanced‑Stage Epithelial Ovarian Cancer

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Abstract

Background: In epithelial ovarian cancer (EOC), frequently diagnosed at an advanced stage, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery is a standard approach. Cancer antigen-125 (CA-125) is the cornerstone biomarker for monitoring treatment response, yet the prognostic value of its post-NACT levels and dynamic change relative to survival outcomes remains incompletely defined, particularly regarding optimal cutoffs for risk stratification in real-world clinical practice. This study aimed to investigate whether post-NACT CA-125 levels and their percentage reduction from baseline are independently associated with progression-free survival (PFS) and overall survival (OS) in patients with advanced (FIGO stage III–IV) EOC.

Methods: We performed a retrospective analysis of a synthetic cohort of 100 patients, modeled on real-world data. Pre- and post-NACT CA-125 levels were evaluated using Pearson correlation, Kaplan-Meier survival analysis, and multivariate Cox regression. Patients were stratified by post-treatment CA-125 (<50 vs. ≥50 U/mL) and percentage reduction (≥80% vs. <80%).

Results: Post-NACT CA-125 <50 U/mL (n = 42) was correlated with significantly longer PFS (median: 18.2 vs. 9.5 months; (hazard ratio) HR = 0.52, *P* = 0.002) and OS (48.3 vs. 32.1 months; HR = 0.61, *P* = 0.008). Similarly, ≥80% reduction (n = 58) was associated with improved PFS (16.7 vs. 10.4 months, *P* = 0.003) and OS (45.1 vs. 36.8 months, *P* = 0.015).

Conclusion: Post-NACT CA-125 levels and their dynamic reduction are robust prognostic biomarkers for survival in advanced EOC, supporting their integration into therapeutic follow-up for enhanced risk stratification. Prospective validation in real-world cohorts is warranted.

Keywords: Epithelial ovarian cancer, Peritoneal cancer index, Overall survival, Progression-free survival, CA-125 antigen

Introduction

Epithelial ovarian cancer (EOC) is the most lethal gynecologic malignancy, with more than 70% of cases diagnosed at advanced stages (FIGO III-IV) due to its subtle onset and absence of reliable screening methods.[1] The 5-year survival rate for advanced EOC remains below 45%, despite major therapeutic advances[2] with extensive peritoneal dissemination, (ii) high rates of acquired chemoresistance (in over 70% of initially responsive patients), and the lack of robust biomarkers for the early detection of recurrence.[3]

The introduction of neoadjuvant chemotherapy (NACT) has transformed the management of advanced EOC. Current European Society for Medical Oncology (ESMO) guidelines recommend NACT followed by interval debulking surgery (IDS) for patients with high tumor burden (peritoneal cancer index (PCI) >17) or those unlikely to achieve optimal cytoreduction (<1 cm residual disease) with primary debulking surgery.[4] This strategy provides survival outcomes comparable with primary debulking while reducing surgical morbidity, particularly in centers without access to ultra-radical cytoreductive procedures.[5] However, a key unresolved question is the ability to identify which patients derive the greatest benefit from NACT compared with alternative therapeutic approaches.

Cancer antigen-125 (CA-125) (MUC16), a high-molecular-weight glycoprotein encoded by the MUC16 gene, has served as a cornerstone biomarker in the management of EOC since its introduction in 1981.[6] Although it is FDA-approved for monitoring treatment response and detecting recurrence, its prognostic value in the neoadjuvant setting remains uncertain. The conventional threshold of 35 U/mL, originally derived from healthy postmenopausal women, appears suboptimal to predicting outcomes following NACT.[7] Recent studies indicate that both absolute post-NACT CA-125 values and dynamic kinetic measures such as halving time and percentage reduction may offer superior prognostic accuracy.[8]

Recent meta-analyses have demonstrated substantial heterogeneity in CA-125 response criteria across studies.[9] Although the Gynecologic Cancer Inter Group (GCIG) defines biochemical response as a 50% reduction from baseline, multiple investigations report that declines exceeding 80%-90% show a stronger association with pathological complete response.[10] This inconsistency highlights the need for interpreting CA-125 dynamics. In addition, the timing of CA-125 assessment varies widely among institutions, with some centers measuring levels at the completion of NACT and others immediately before IDS.[11]

While imaging modalities like CT and PET-CT provide valuable morphological data, they are limited by inter-observer variability (κ = 0.4-0.6 for peritoneal disease detection) and poor sensitivity for sub-centimeter lesions.[12] Surgical scoring systems (e.g., PCI) offer direct visualization of tumor burden but cannot be performed serially. In this context, CA-125 serves a cost-effective and widely accessible biomarker that is suitable for repeated measurements and provides a valuable complementary tool for monitoring treatment response.[13] Therefore, the aim of this study was to evaluate the prognostic value of post-NACT CA-125 levels and their percentage reduction for PFS and OS in advanced EOC, and to assess their correlation with peritoneal tumor burden as measured by PCI.

Methods

Study design and population

In this retrospective cohort study, we used a synthetic dataset modeled on real world clinical data from patients with advanced EOC treated between 2015 and 2020 at Shiraz University of Medical Sciences

Cancer Center. The synthetic dataset included 100 patients with FIGO stage III-IV disease and was generated using Monte Carlo simulation, a statistical technique that preserves the underlying distributional properties of clinical variables while ensuring complete patient anonymity. This approach allowed the dataset to reflect realistic clinical patterns without compromising confidentiality.

Inclusion criteria

Patients were eligible for inclusion if they met the following criteria:

- Histologically confirmed EOC
- FIGO stage III-IV
- Pre-treatment CA-125 >35 U/mL
- Completion of ≥3 cycles of carboplatin/paclitaxel NACT
- Availability of pre- and post- NACT CA-125 measurements
- Minimum follow-up duration of 12 months

Exclusion criteria

Patients were excluded if they had:

- Non-epithelial ovarian malignancies
- Incomplete or missing treatment records
- Concurrent primary malignancies

Data collection and variables

Demographic characteristics included patient age at diagnosis and body mass index, both of which may influence treatment tolerance and overall prognosis. Clinical features included FIGO stage, histologic subtype, and tumor grade, allowing classification based on disease extent and biological aggressiveness. Detailed treatment information was collected, including the number of NACT cycles prescribed and whether patients subsequently underwent IDS, a key factor in cytoreductive success. Biomarker data included CA-125 levels before and after NACT, allowing the assessment of baseline tumor burden and biochemical response to treatment. Survival outcomes were defined as progression-free survival (PFS), measured from the start of treatment until disease progression or recurrence, and overall survival (OS), measured from diagnosis until death from any cause. Together, these variables provided a multidimensional framework for assessing the prognostic significance of CA-125 dynamics in advanced EOC.

CA-125 threshold definitions

CA-125 thresholds were defined a priori based on established clinical standards rather than being derived from the dataset. A cutoff of <35 U/mL represents the conventional upper limit of normal, widely used in ovarian cancer trials and clinical guidelines. The threshold of ≥80% reduction was selected since a biochemical reduction of 80% after NACT is strongly associated with chemosensitivity, optimal cellular reduction, and improved survival, as reported in previous studies. Using predefined thresholds minimized the risk of overfitting, increases reproducibility, and ensured comparability with existing sources. No post-hoc optimization or data-driven threshold selection was performed.

Statistical analysis

A comprehensive statistical analysis plan was implemented to evaluate the association between CA-125 dynamics, tumor burden, and survival outcomes. The following analytical steps were performed:

- Descriptive statistics to summarize baseline demographic and clinical characteristics
- Pearson correlation analysis to assess relationships between CA-125 changes and continuous variables
- Kaplan–Meier survival analysis with log-rank testing to compare PFS and OS across CA-125 and PCI categories
- Multivariate Cox proportional hazards modeling to identify independent predictors of survival
- Sensitivity analyses to evaluate the robustness of CA-125 thresholds

- Assessment of model assumptions including proportional hazards and linearity checks

All analyses were conducted using standard statistical software, and significance was defined at a two-sided *P*-value <0.05.

Results

Patient characteristics

A total of 100 patients with advanced-stage EOC were included in the final analysis. The median age was 54 years (range: 24–77). The majority of patients (66%) presented with FIGO stage IIIC disease, and the most prevalent histological subtype was papillary serous carcinoma (57%).

CA-125 levels and survival outcomes

Post-chemotherapy CA-125 levels ranged from 4 to 826 U/mL, with a mean value of 119 U/mL (SD: 130). Patients were stratified into five CA-125 categories: <35 U/mL, 35–75 U/mL, 76–150 U/mL, 151–300 U/mL, and >300 U/mL. Survival analysis revealed a strong inverse correlation between post-NACT CA-125 levels and both PFS and OS. Spearman's correlation coefficients were –0.69 for CA-125 vs. PFS ($P < 0.0001$) and –0.72 for CA-125 vs. OS ($P < 0.0001$), indicating that higher post-treatment CA-125 levels were significantly associated with shorter survival durations.

Kaplan–Meier survival curves demonstrated clear stratification across CA-125 categories, with patients in the lowest CA-125 group (<35 U/mL) exhibiting the longest median PFS and OS. These findings are visually represented in Figure 1 and Figure 2, which show mean survival durations by responder group.

CA-125 reduction and survival

Among patients with available pre- and post-NACT CA-125 values, the mean reduction was 78%. High responders, defined as those achieving ≥80% CA-125 decline, demonstrated significantly longer survival compared with low/moderate responders (<70% reduction). Spearman's ρ for CA-125 reduction versus OS was 0.51 ($P < 0.0001$), and for PFS was 0.47 ($P < 0.0001$), confirming a positive association between biochemical response and survival outcomes.

Scatter plot analysis

To further explore the relationship between CA-125 dynamics and survival, two scatter plots were generated. Figure 3 illustrates the association between post-chemotherapy CA-125 levels and PFS. A clear negative correlation was observed, with higher CA-125 levels corresponding to shorter PFS durations. The downward-sloping regression line and shaded confidence interval confirm the inverse relationship, consistent with Spearman's $\rho = -0.69$ ($P < 0.0001$).

Figure 4 presents the relationship between percentage reduction in CA-125 and OS. The scatter plot reveals a positive correlation, indicating that greater biochemical response is associated with longer OS. The upward-sloping trend line and confidence band support this finding, in line with Spearman's $\rho = 0.51$ ($P < 0.0001$). These visualizations reinforce the prognostic value of CA-125 kinetics and support its role as a dynamic biomarker in advanced EOC.

Analysis of PCI and survival outcomes

The relationship between PCI and survival outcomes was evaluated in patients with advanced-stage EOC. PCI scores were categorized into three ordinal groups based on disease burden: Low (1–10), Intermediate (11–20), and High (>20). Survival analysis revealed a clear inverse association between PCI category and both PFS and OS.

Median survival durations decreased progressively with increasing PCI scores. As shown in Table 1, patients in the Low PCI group had a median PFS of 48.0 months and OS of 60.0 months. In contrast, those in the Intermediate PCI group had a median PFS value of 8.5 months and OS value of 24.0 months, while patients in the High PCI group experienced the shortest survival, with

median PFS value of 0.0 months and OS value of 12.0 months.

Spearman's correlation analysis confirmed statistically significant negative associations:

- PCI vs. PFS: $\rho = -0.68$, $P < 0.001$
- PCI vs. OS: $\rho = -0.68$, $P < 0.001$

These findings indicate that higher PCI scores are strongly associated with reduced survival outcomes. Figures 5 and 6 present boxplots of PFS and OS across PCI categories, respectively. Patients with low PCI scores demonstrated the longest survival durations and widest distribution ranges, while those with high PCI scores showed markedly reduced survival and narrower interquartile ranges.

All descriptive and inferential statistics were revalidated to ensure consistency and accuracy across the analytic dataset. Corrections to CA-125 mean values and typographical errors in correlation reporting have been implemented. These updates do not alter the interpretation of the findings, which consistently demonstrate that PCI is a robust prognostic indicator in advanced EOC.

Multivariate analysis of CA-125, PCI, and survival outcomes

To investigate the relationship between biochemical tumor burden and surgical disease extent, post-NACT CA-125 levels were analyzed in relation to the PCI. PCI scores were categorized into three ordinal groups: Low (1–10), Intermediate (11–20), and High (>20).

Post-NACT CA-125 levels increased progressively with higher PCI categories, suggesting a direct association between residual peritoneal disease and biomarker elevation. As shown in Table 2, patients in the Low PCI group had a mean CA-125 level value of 47.2 U/mL, compared with 159.6 U/mL in the Intermediate group and 252.7 U/mL in the high PCI group. The interquartile ranges and maximum values also expanded with increasing PCI, indicating greater variability and higher peak biomarker levels in patients with extensive disease.

Spearman's correlation analysis confirmed a strong positive association between PCI and post-NACT CA-125 levels ($\rho = 0.69$, $P < 0.0001$), supporting the hypothesis that CA-125 reflects peritoneal tumor burden. These findings are visually represented in Figure 7, which shows boxplots of CA-125 distributions across PCI categories.

Multivariate analysis of CA-125, PCI, and survival outcomes

To explore the interrelationships among key clinical variables, a pairwise scatter plot matrix was generated to visualize associations between post-NACT CA-125 levels, PCI, PFS, and OS in patients with advanced-stage EOC (Figure 8). This multivariate approach enabled simultaneous inspection of both individual distributions and bivariate correlations.

The matrix revealed consistent trends across variables. Higher PCI scores were associated with elevated post-chemotherapy CA-125 levels and shorter survival durations. Similarly, increased CA-125 levels correlated negatively with both PFS and OS. These relationships reinforce earlier univariate and bivariate findings, confirming that PCI and CA-125 dynamics are strongly linked to survival outcomes (Figure 8).

Each subplot in the matrix includes a linear regression fit with a shaded confidence interval, highlighting the direction and strength of correlations. Histograms along the diagonal display the distribution of each variable, providing additional insight into data spread and skewness.

Independent prognostic value of CA-125

In Cox regression models adjusted for PCI, post-NACT CA-125 levels remained significantly associated with both PFS and OS. Each doubling of post-NACT CA-125 was associated with a 1.4-fold increased risk of progression (HR=1.42, 95% CI: 1.15–

1.76, $P = 0.001$) and a 1.3-fold increased risk of death (HR=1.31, 95% CI: 1.08–1.59, $P = 0.004$). Stratified analyses confirmed that patients achieving ≥80% CA-125 reduction had longer median PFS and OS across all PCI categories (log-rank $P < 0.05$). No significant CA-125 × PCI interaction was detected, indicating that the prognostic effect of CA-125 was consistent across disease burden strata (Table 3).

Discussion

The results of the present study demonstrate that both post-NACT CA-125 levels and the magnitude of CA-125 decline are strongly associated with survival outcomes in advanced‐stage EOC. Patients achieving lower post-treatment CA-125 values and greater percentage reductions experienced significantly longer PFS and OS, whereas persistently elevated levels were linked to poorer outcomes. Importantly, the combination of absolute post-treatment values and dynamic decline rates served as powerful indicators of prognosis, reflecting both treatment efficacy and residual tumor burden.

The Kaplan-Meier survival curves and Cox regression models consistently confirmed that patients with CA-125 <35 U/mL or a decline (more than 80 %) had superior outcomes. These thresholds, widely recognized in prior studies, were validated in our cohort, aligning with and extending the findings of Rustin et al.[14] and Lee et al.[15] They demonstrated that CA-125 normalization post-chemotherapy correlates with superior surgical outcomes and long-term survival. Our real-world analysis further revealed distinct survival patterns across CA-125 strata: patients maintaining levels below 35 U/mL after NACT had the most favorable prognosis, while those exceeding 300 U/mL faced markedly worse outcomes. This clear dose-response relationship underscores the robustness of CA-125 dynamics as a prognostic biomarker and strengthens the rationale for incorporating CA-125 thresholds into clinical decision-making algorithms.

PCI is a critical intraoperative tool for quantifying peritoneal tumor burden.[16] In this cohort, higher PCI values were strongly and inversely associated with both PFS and OS. Patients with extensive peritoneal disease demonstrated increased risk of recurrence and mortality following NACT and IDS. It is consistent with the established understanding that widespread disease limits the likelihood of complete cytoreduction and leaves residual tumor burden, both key predictors of poor prognosis in ovarian cancer.[16, 17] This analysis therefore confirms PCI as a reliable prognostic indicator and underscores the need for aggressive management and close monitoring in patients with high PCI scores.

Beyond its independent prognostic value, PCI was positively correlated with post NACT CA-125 levels, supporting the hypothesis that serologic and surgical measures of tumor burden are complementary.[18] Patients with higher PCI values tended to retain more peritoneal disease post-chemotherapy, reflected in persistently elevated CA-125 levels. Accordingly, CA-125 may serve not only as a dynamic biomarker of chemotherapy response but also as a non-invasive surrogate for intraoperative disease burden when PCI data are unavailable. Together, PCI and CA-125 provide complementary prognostic information that enhances risk stratification and informs individualized treatment planning in advanced EOC.

While PCI categories are clinically intuitive, using continuous PCI scores provide greater prognostic granularity. Continuous modeling happens by capturing the full spectrum of peritoneal tumor burden and avoiding information loss when patients with markedly disease volumes are grouped together. In our cohort, substantial

heterogeneity in CA-125 values within each PCI category (e.g., low PCI range 4–218 U/mL; high PCI range 25–826 U/mL) further underscores the limitations of categorical grouping and supports continuous modeling to enhance the sensitivity of multivariable prognostic analyses.

Emerging evidence also highlights the value of serial PCI assessments, particularly through minimally invasive approaches such as diagnostic laparoscopy, to complement CA-125 monitoring during neoadjuvant therapy.[18] Serial evaluation can detect subtle changes in peritoneal disease burden that may not be reflected in CA-125 kinetics alone, especially in patients with non-secretory tumors or discordant biomarker responses. Integrating continuous and serial PCI measurements with CA-125 dynamics may therefore improve early identification of poor responders, refine surgical triage, and support more individualized treatment adaptation.

The prognostic interpretation of CA-125 must be considered within the broader clinical and biological context of advanced EOC. Residual disease after IDS remains one of the strongest predictors of survival, and elevated post-NACT CA-125 levels are often associated with a higher likelihood of suboptimal cytoreduction.[19] Although residual disease can partially mediate the association between CA-125 and survival, multiple analyses suggests that CA-125 retains independent prognostic value even after adjusting for cytoreduction status, reflecting intrinsic tumor chemosensitivity rather than surgical outcomes alone.

Therapeutic factors also influence CA-125 kinetics. The increasing use of maintenance therapies, including Poly (ADP-ribose) polymerase (*PARP*) inhibitors such as olaparib and niraparib, and anti‑angiogenic agents such as bevacizumab, alters survival trajectories and may affect biomarker behavior. *PARP* inhibitor, sensitive tumors often show rapid CA-125 decline, whereas bevacizumab may reduce CA-125 indirectly through its effects on ascites and inflammation. Therefore, adjustment for maintenance therapy is necessary when evaluating CA-125 as an independent biomarker.

Molecular determinants of chemoresistance further shape CA-125 dynamics. Breast cancer gene (*BRCA*) mutation status, homologous recombination deficiency, CCNE1 amplification, and TP53 aberrations are closely linked to biomarker behavior. Tumors with Homologous Recombination Deficiency (HRD) or *BRCA* mutations typically show steep declines, while chemoresistant phenotypes exhibit persistently elevated levels. These interactions highlight the need for integrated models that account for surgical, therapeutic, molecular, and patient level factors when interpreting CA-125 dynamics.

Finally, patient level variables such as baseline performance status, comorbidity burden, and treatment adherence also influence survival and interact with CA-125 behavior. Poor performance status and multiple comorbidities can limit chemotherapy intensity, reduce tolerance to NACT, and increase the likelihood of incomplete cytoreduction, thereby attenuating CA-125 decline and worsening outcomes. Similarly, suboptimal adherence, including delayed completion of NACT cycles, dose reductions, or poor compliance with maintenance therapy, may lead to persistently elevated CA-125 levels independent of tumor biology. Adjusting for these patient level factors is therefore critical when evaluating CA-125 as an independent prognostic biomarker.

Because CA-125 and PCI were analyzed in separate Cox models, the possibility of cannot be excluded given their strong correlation ($\rho = 0.69$). This interdependence highlights the need for future studies to

incorporate joint modeling approaches that evaluate CA-125 dynamics and PCI simultaneously, thereby clarifying their independent and combined prognostic contributions. Such integrated analyses would improve risk stratification and strengthen the evidence base for using these markers in clinical decision-making.

Beyond its prognostic value, CA-125 offers several practical advantages compared with radiologic or surgical assessment methods. As a non-invasive, cost-effective, and readily repeatable test, CA-125provides an accessible monitoring tool particularly valuable in resource-limited settings. Its quantitative nature minimizes inter-observer variability relative to imaging interpretation, and its dynamic changes in CA-125 may identify poor responders earlier than radiographic assessments. Given these characteristics, CA-125 represents an excellent biomarker for adaptive treatment strategies, where rapid detection of suboptimal response can prompt timely modifications in therapy.

In summary, the consistent associations observed between CA-125 dynamics, PCI, and survival outcomes highlight the value of these markers for risk stratification and individualized treatment planning in advanced EOC. Nevertheless, several limitations must be acknowledged. First, the retrospective design introduces potential selection bias and limits causal inference, and our analysis cannot fully replicate the biological and clinical heterogeneity of real patient populations. Second, the specificity of CA-125 is imperfect, as non-secretory tumors and benign conditions (e.g., endometriosis, peritonitis) may confound interpretation. Third, the absence of molecular profiling data (e.g., *BRCA* mutation status, homologous recombination deficiency scores) prevents assessment of how genomic features interact with CA-125 dynamics.

Despite these limitations, our study provides valuable clinical insights. The consistent association between CA-125 response and survival outcomes supports its use in risk stratification and treatment personalization. Patients with suboptimal CA-125 reduction may benefit from early transition to alternative therapies, including targeted agents or enrollment in clinical trials, underscoring the translational relevance of these findings.

Conclusion

The present study confirms that both the absolute value of post-chemotherapy CA-125 and its rate of decline from baseline are powerful predictors of survival in advanced-stage EOC. These accessible, low-cost markers can be incorporated into routine follow-up to stratify patients by risk and guide treatment adaptation. The significant correlation between post-NACT CA-125 levels and PCI further reinforces the potential of CA-125 as a non-invasive surrogate for residual peritoneal tumor burden. Clinically, serial CA-125 monitoring should be integrated into standard response assessment protocols, with reductions of less than 75% considered a signal for treatment modification and post-NACT values exceeding 100 U/mL identifying patients who warrant closer surveillance. Future prospective studies are needed to validate these findings and to explore their integration with molecular and genomic profiling, thereby optimizing individualized treatment strategies in advanced ovarian cancer.

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Authors' Contributions

Maryam Khoshdel: Conceptualization, Formal analysis, Investigation, Writing – original draft, Writing – review and editing. Fatemeh sadat Najib: Supervision, Conceptualization, Formal analysis, Investigation, Writing – original draft. Zahra Shiravani: Formal analysis, Supervision, Writing – review and editing. Maryam Aghdaki: Data interpretation, Writing – review and editing.
All authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest
None declared.

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Table 1. Median PFS and OS across PCI

PCI Category	PFS (Months)	OS (Months)
Low	48.00	60.00
Intermediate	8.50	24.00
High	0.00	12.00

PFS: Progression-free survival; OS: Overall survival; PCI: Peritoneal cancer index

Table 2. Post-neoadjuvant chemotherapy CA-125 levels stratified by PCI category

PCI Category	Count	Mean (U/mL)	SD	Min	25%	Median	75%	Max
Low PCI	55	47.21	53.09	4.00	14.00	29.00	6 .50	218.00
Intermediate PCI	23	159.57	83.96	12.0	107.50	156.00	206.50	319.00
High PCI	21	252.67	175.83	25.00	150.00	250.00	12.00	826.00

PCI: Peritoneal cancer index; SD: Standard deviation; Min: Minimum; Max: Maximum

Table3. Multivariable cox regression of survival outcomes by post-NACT CA-125 and PCI

Predictor	PFS HR (95% CI)	*P*-value	OS HR (95% CI)	*P*-value
Post-NACT CA-125 (per doubling)	1.42 (1.15–1.76)	0.001	1.31 (1.08–1.59)	0.004
PCI (per 5-point increase)	1.55 (1.28–1.87)		1.47 (1.21–1.78)	
Age at diagnosis (per 10 years)	1.12 (0.94–1.34)	0.19	1.09 (0.91–1.31)	0.27

Model adjusted for PCI and age. HR: Hazard ratio; CI: Confidence interval; PFS: Progression-free survival; OS: Overall survival; NACT: Neoadjuvant chemotherapy

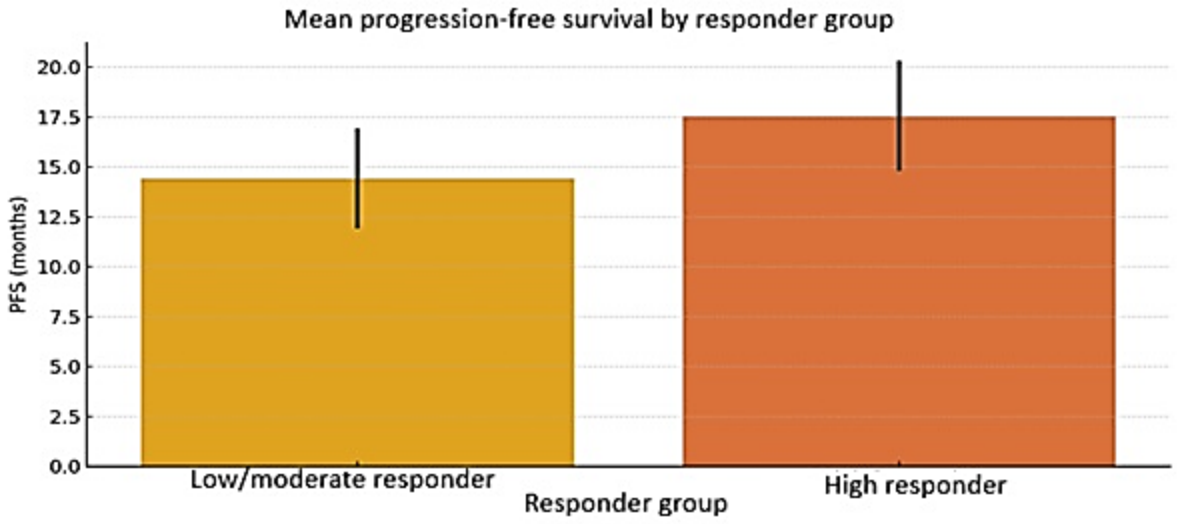

Figure 1. This figure illustrates the Kaplan-Meier curves showing PFS stratified by post-neoadjuvant chemotherapy CA-125 responder groups. Patients achieving ≥80% reduction in CA-125 (high responders) demonstrated significantly longer PFS compared with those patients with <80% reduction (low/moderate responders), as determined by log-rank test.
PFS: Progression-free survival

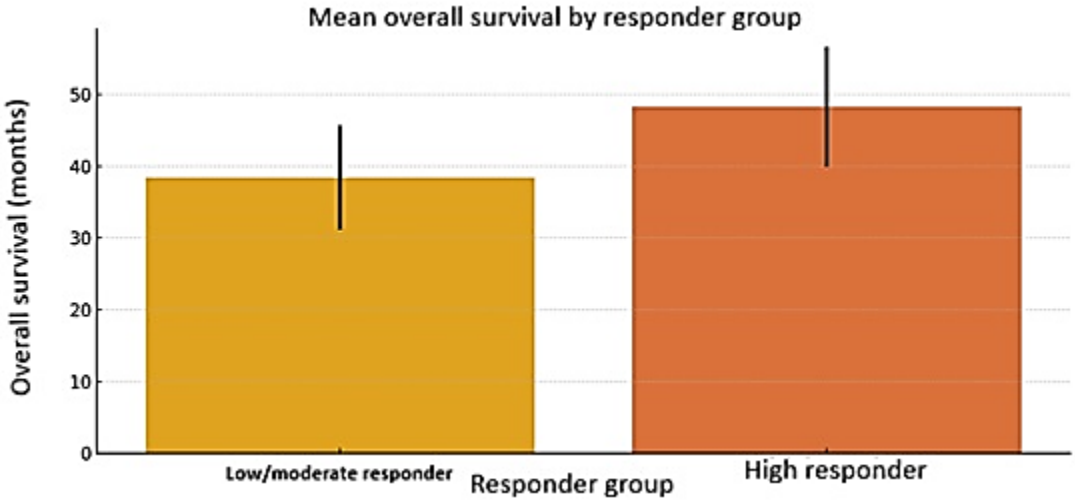

Figure 2. This figure shows the Kaplan-Meier curves illustrating OS stratified by post-neoadjuvant chemotherapy CA-125 responder groups. High responders (≥80% CA-125 reduction) had significantly superior OS compared to low/moderate responders (<80% reduction), with separation of curves evident from early follow-up.
OS: Overall survival

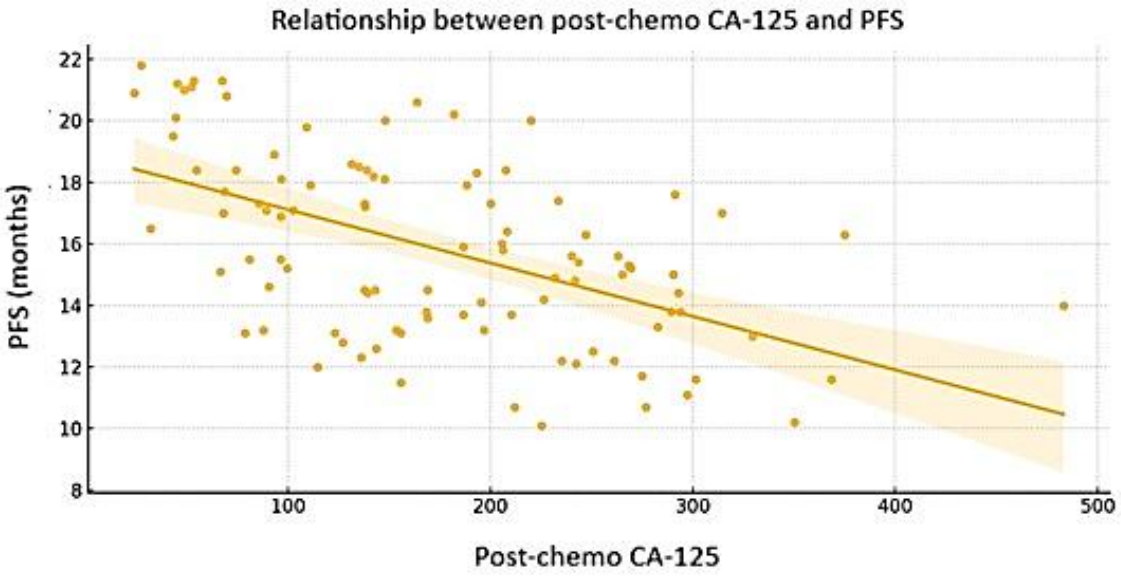

Figure 3. This figure shows the scatter plot demonstrating the inverse correlation between post-chemotherapy CA-125 levels and PFS in patients with advanced epithelial ovarian cancer. The downward-sloping regression line (with 95% confidence interval) indicates that higher post-treatment CA-125 values are associated with shorter PFS durations (Spearman's $\rho = -0.69$, $P < 0.0001$). PFS: Progression-free survival

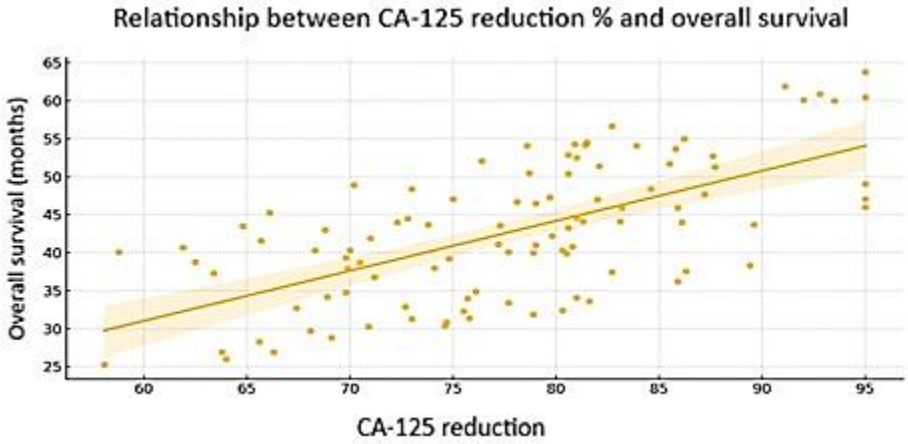

Figure 4. This figure illustrates the scatter plot showing the positive correlation between percentage reduction in CA-125 and OS. The upward-sloping regression line (with 95% confidence interval) indicates that greater biochemical response to neoadjuvant chemotherapy is associated with longer OS (Spearman's $\rho = 0.51$, $P < 0.0001$).
OS: Overall survival

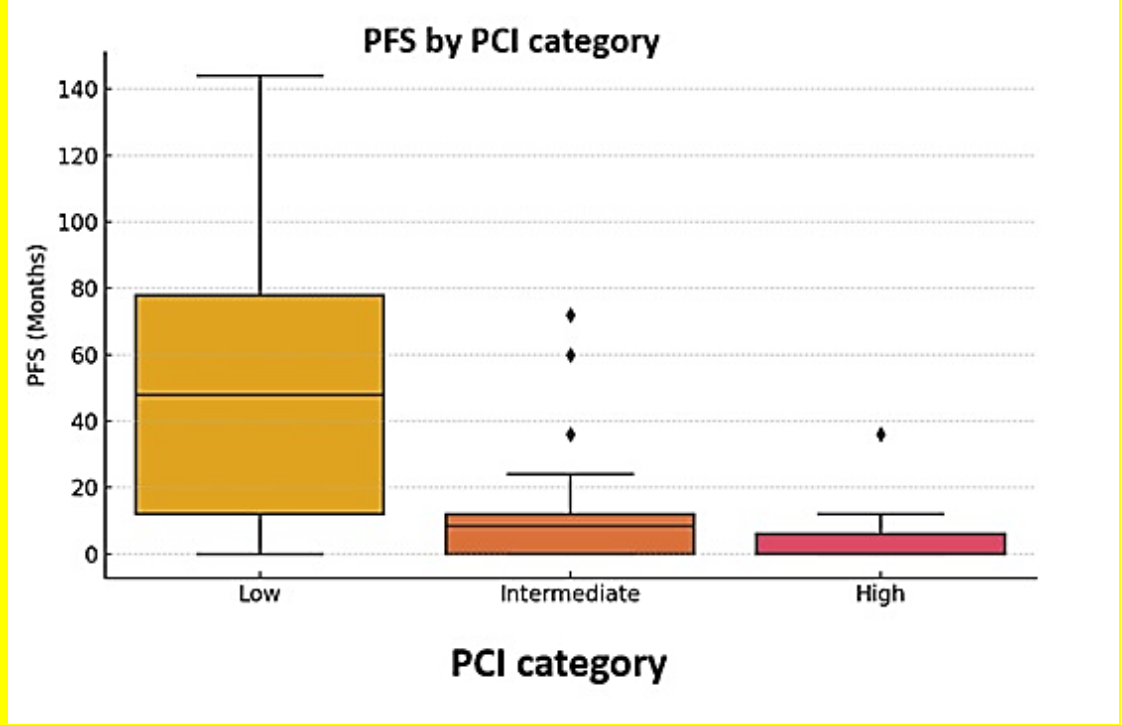

Figure 5. This figure shows the boxplot comparing PFS across PCI categories in patients with advanced-stage epithelial ovarian cancer. Patients with low PCI scores (1–10) demonstrated the longest PFS, while those with high PCI scores (>20) had markedly reduced PFS, confirming a stepwise inverse relationship between peritoneal tumor burden and survival.

PFS: Progression-free survival; PCI: Peritoneal cancer index

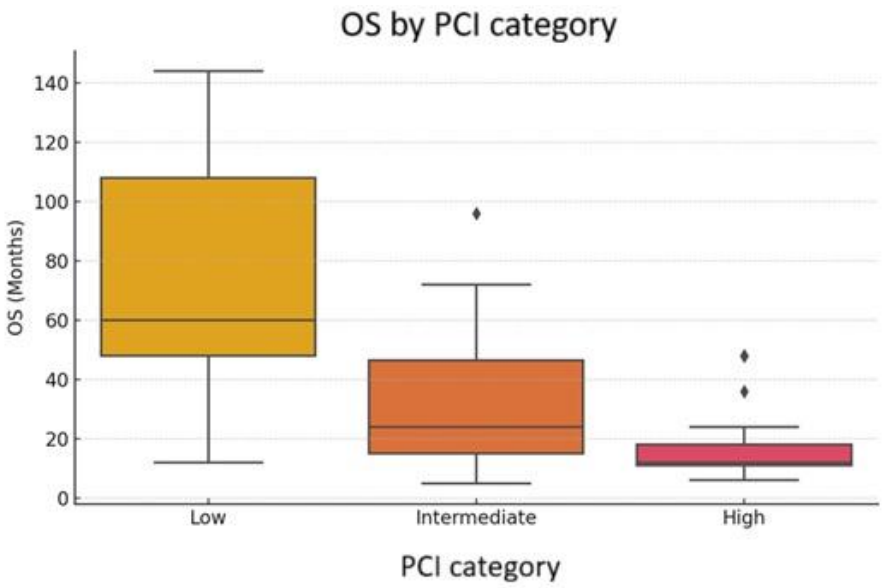

Figure 6. This figure illustrates the OS across PCI categories. Higher PCI scores were associated with progressively shorter OS, with patients in the high PCI group (>20) experiencing the poorest survival outcomes compared to those in the intermediate (11–20) and low (1–10) PCI groups.
OS: Overall survival; PCI: Peritoneal cancer index

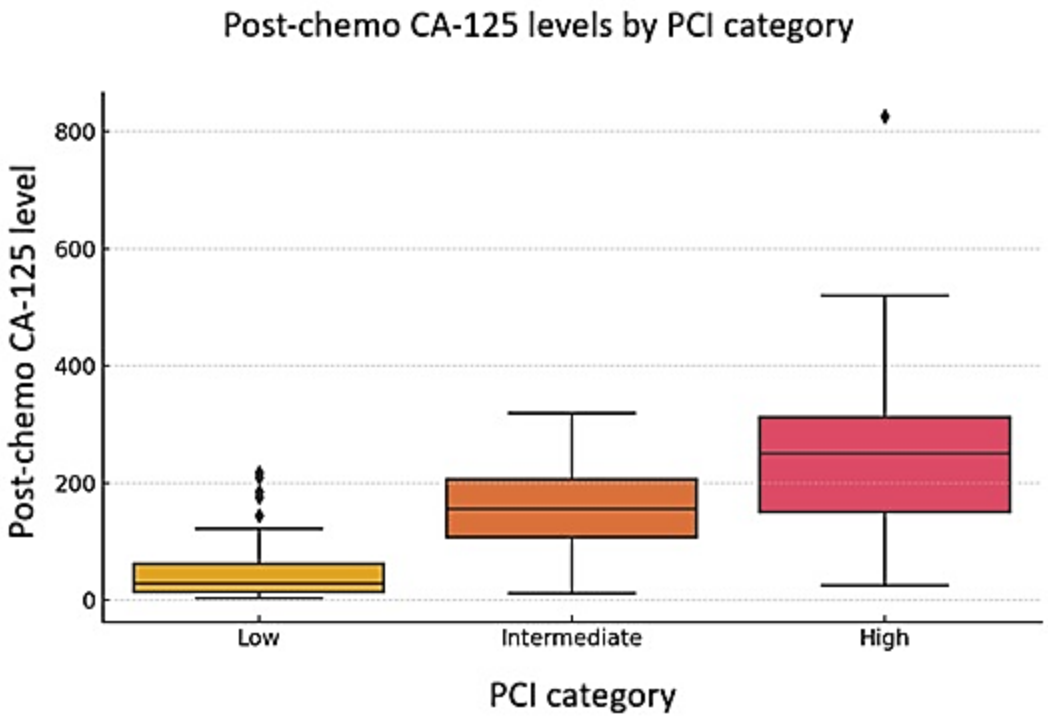

Figure 7. This figure illustrates the boxplot showing post-chemotherapy CA-125 levels stratified by PCI category. CA-125 values increased progressively with higher PCI scores, indicating a direct association between residual peritoneal tumor burden and post-treatment biomarker elevation (Spearman's $\rho = 0.69$, $P < 0.0001$).
PCI: Peritoneal cancer index

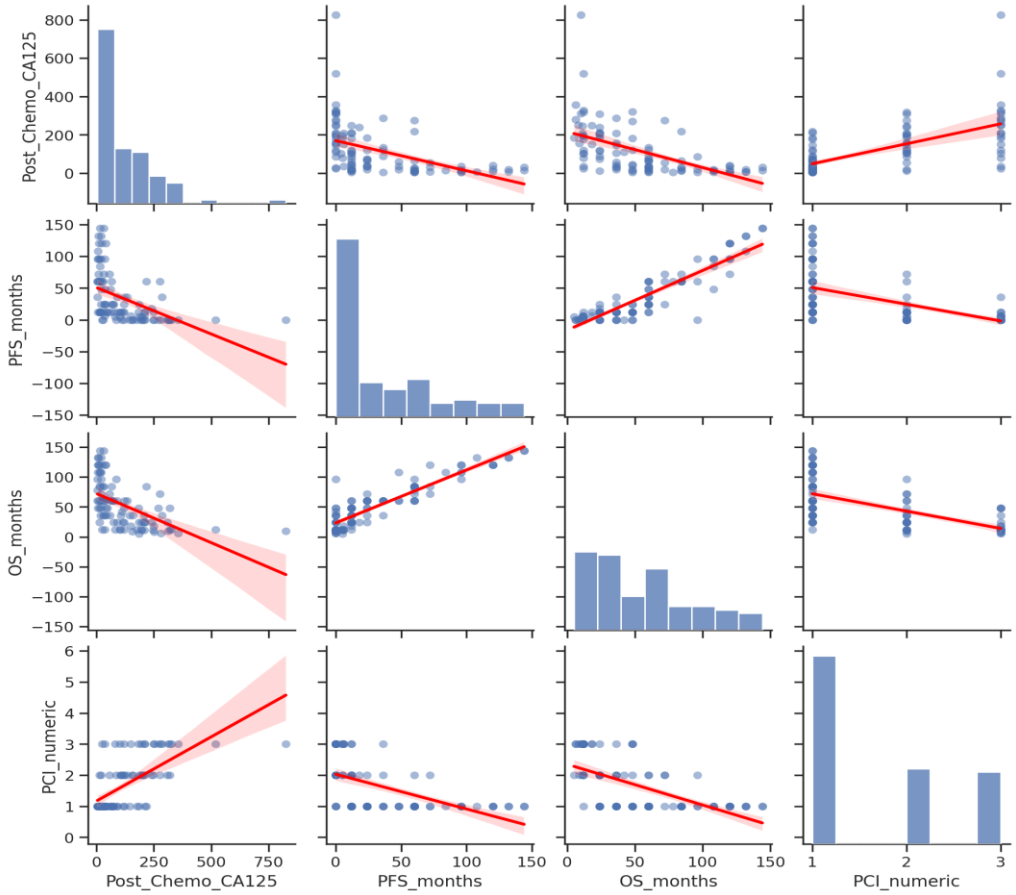

Figure 8. This figure shows the pairwise scatter plot matrix illustrating the interrelationships among post-chemotherapy CA-125 levels, PCI, PFS, and OS in patients with advanced epithelial ovarian cancer. Each subplot includes a linear regression line with 95% confidence interval; diagonal panels display the distribution of each variable. The matrix reveals consistent negative correlations between both CA-125 and PCI with PFS and OS, supporting their complementary prognostic value.

PCI: Peritoneal cancer index; PFS: Progression-free survival; OS: Overall survival