

## Chemotherapy Response Score Following Neoadjuvant Chemotherapy and its Association with Surgical Outcome and Early Prognosis in Advanced Epithelial Ovarian Cancer: A Single-Center Study

Susmita Sarker<sup>1</sup>, Shahana Pervin<sup>2</sup>, Sadia Jabeen Khan<sup>3</sup>, Farhana Haque<sup>4</sup>, Dilruba Yeasmin<sup>5</sup>, Rumana Afroz<sup>6</sup>, Mst Rukshana Pervin<sup>7</sup>

<sup>1</sup>Junior Consultant, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [drsarker11@gmail.com](mailto:drsarker11@gmail.com)

<sup>2</sup>Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [shahana.pervin@yahoo.com](mailto:shahana.pervin@yahoo.com)

<sup>3</sup>Associate Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [sjabeen326@gmail.com](mailto:sjabeen326@gmail.com)

<sup>4</sup>Assistant Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [farhananila77@gmail.com](mailto:farhananila77@gmail.com)

<sup>5</sup>Assistant Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [deenacmc113@gmail.com](mailto:deenacmc113@gmail.com)

<sup>6</sup>Assistant Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh; Email: [rumanaafroz12@gmail.com](mailto:rumanaafroz12@gmail.com)

<sup>7</sup>Junior Consultant, Kurmitola General Hospital, Dhaka, Bangladesh; Email: [d.pervin01@yahoo.com](mailto:d.pervin01@yahoo.com)

**Corresponding Author:** Dr. Susmita Sarker, Junior Consultant, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh

Email: [drsarker11@gmail.com](mailto:drsarker11@gmail.com)

### ABSTRACT

**Background:** Chemotherapy response score (CRS) is a histopathologic measure of tumor regression following neoadjuvant chemotherapy (NACT) in advanced epithelial ovarian cancer. Evidence from resource-limited settings remains limited. This study aimed to evaluate the association of CRS with surgical cytoreduction, platinum resistance, disease progression, and survival following NACT and interval debulking surgery (IDS).

**Methods:** This prospective observational cohort included 153 women with FIGO stage III–IV epithelial ovarian cancer treated at NICRH, Dhaka, from January 2017 to December 2019, with follow-up through December 2022. All patients received paclitaxel–carboplatin NACT followed by IDS. CRS was assigned using a three-tier system and categorized as CRS 1–2 versus CRS 3. Group comparisons were performed using t-tests and chi-square or Fisher’s exact tests. Logistic regression assessed progression at 1 and 3 years, while progression-free survival (PFS) was analyzed using Kaplan–Meier curves with log-rank testing.

**Results:** Among 153 patients, 126 were CRS 1–2 and 27 were CRS 3. R0 resection was achieved in 88.9% of CRS 3 compared with 35.7% of CRS 1–2 ( $p < 0.001$ ). Platinum resistance occurred in 54.8% of CRS 1–2 and none in CRS 3 ( $p < 0.001$ ). One- and three-year survival rates were significantly higher in CRS 3. CRS 1–2 and residual disease independently predicted progression, while PFS was significantly improved in CRS 3.

**Conclusion:** CRS is a strong predictor of cytoreduction, platinum sensitivity, progression risk, and survival outcomes after NACT–IDS in advanced ovarian cancer.

**Keywords:** Chemotherapy Response Score, Neoadjuvant Chemotherapy, High-Grade Serous Ovarian Carcinoma, Interval Debulking Surgery, Progression-Free Survival

**How to Cite:** Susmita Sarker, Shahana Pervin, Sadia Jabeen Khan, Farhana Haque, Dilruba Yeasmin, Rumana Afroz, Mst Rukshana Pervin, (2026) Chemotherapy Response Score Following Neoadjuvant Chemotherapy and its Association with Surgical Outcome and Early Prognosis in Advanced Epithelial Ovarian Cancer: A Single-Center Study, *Journal of Carcinogenesis*, Vol.25, No.1, 443-451

## 1. INTRODUCTION

Epithelial ovarian cancer (EOC) remains one of the most lethal gynecologic malignancies worldwide, accounting for a substantial proportion of cancer-related deaths among women despite advances in diagnosis and therapy. Globally, ovarian cancer ranks as the eighth most common cancer among females and the fifth leading cause of cancer-related mortality (1). Late-stage presentation continues to predominate, particularly in low- and middle-income countries, where limited awareness and diagnostic access contribute to delayed detection and poor survival outcomes (2). More than 90–95% of ovarian cancers are of epithelial origin, and the majority are diagnosed at FIGO stage III or IV, when disease dissemination beyond the pelvis is extensive and curative surgery is often not immediately feasible (3). The global burden data indicate that, despite the incorporation of taxane–platinum combinations and improved surgical techniques, overall survival rates have plateaued, emphasizing the persistent need for effective multimodal management strategies (1,2).

For advanced-stage disease, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) has become an established therapeutic approach, complementing or replacing primary debulking surgery in selected patients (4). NACT aims to reduce tumor bulk, enhance resectability, and improve perioperative outcomes while maintaining oncologic efficacy (5). Large multicenter and randomized trials have demonstrated that, when appropriately applied, NACT followed by IDS achieves similar survival outcomes to primary debulking surgery, but with reduced operative morbidity and improved rates of complete cytoreduction (6,7). The GOTIC-019 study, for instance, confirmed the clinical utility of NACT-IDS in real-world practice, with optimal cytoreduction rates exceeding 70% and acceptable perioperative safety (6). Similarly, pooled analyses and meta-analyses have reinforced the prognostic equivalence of NACT-IDS compared with primary surgery while highlighting its superior surgical tolerability (7,8). As such, the NACT-IDS paradigm has become the preferred strategy for patients with extensive peritoneal spread or poor performance status, where achieving complete macroscopic resection in the upfront setting is unlikely (4).

Despite its widespread adoption, a critical challenge in managing patients undergoing NACT-IDS is the reliable assessment of chemotherapy response. Conventional evaluation methods, radiologic imaging and serum biomarkers such as CA-125, are limited by their inability to fully capture the biological and histopathologic extent of response (9). CA-125, while useful for monitoring trends, can be influenced by tumor histology, non-malignant conditions, and treatment-induced changes unrelated to tumor burden, leading to potential misclassification of responders (9). Similarly, radiologic assessment using RECIST or metabolic imaging may not accurately differentiate viable tumor from post-treatment fibrosis or necrosis, particularly in peritoneal disease where measurable lesions are few (10). These shortcomings underscore the need for more objective and reproducible markers of chemotherapy response that reflect true tumor biology.

The histopathologic examination of post-NACT surgical specimens offers a direct means of assessing the degree of tumor regression and residual viability. To standardize this approach, Böhm and colleagues originally proposed the Chemotherapy Response Score (CRS), a three-tiered histopathologic grading system developed for high-grade serous carcinoma treated with NACT and IDS (11). The CRS incorporates the extent of residual viable tumor and associated fibrosis to classify response as minimal (CRS 1), partial (CRS 2), or complete or near-complete (CRS 3). This standardized scoring system has since been externally validated in multiple cohorts, demonstrating robust reproducibility among pathologists and strong prognostic correlation with progression-free survival and platinum sensitivity (12,13). Notably, CRS has been shown to outperform conventional radiologic and serologic indicators in predicting early recurrence and treatment outcomes, making it an increasingly relevant tool for post-NACT evaluation (14).

Recent reviews have reaffirmed the clinical significance of CRS as both a predictive and prognostic marker in advanced epithelial ovarian cancer, while also highlighting ongoing challenges in standardization, interobserver variability, and application to non-omental sites (15,16). Studies evaluating CRS at multiple anatomical locations have demonstrated that high omental and adnexal CRS scores correlate with improved surgical outcomes and reduced risk of platinum resistance, further supporting its biological and clinical validity (14). However, despite increasing adoption in major centers, CRS data from low- and middle-income countries remain scarce, and region-specific validation of its prognostic impact is limited (15). Given the differences in patient demographics, tumor biology, and treatment infrastructure across global settings, it is essential to evaluate CRS performance in local populations where resource constraints and late presentation are common.

Against this background, the present study aims to assess the association between the chemotherapy response score following neoadjuvant chemotherapy and key clinical outcomes; specifically, surgical cytoreduction and early prognosis, in patients with advanced epithelial ovarian cancer treated at a tertiary referral center in Bangladesh. By correlating CRS categories with residual disease status, platinum resistance, and one-year survival, this study seeks to provide context-specific evidence supporting the prognostic utility of CRS within routine oncologic practice in a resource-limited setting.

## 2. METHODS

### Study design and setting

This prospective observational cohort study was conducted in the Department of Gynecological Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka, Bangladesh. Patient enrollment and baseline data collection were performed from January 2017 to December 2019. Follow-up was continued through December 2022. Ethical approval was obtained from the Ethics Committee of NICRH, Dhaka, Bangladesh (Approval No. NICRH/Ethics/2021/263), and all procedures were conducted in accordance with institutional ethical standards.

### Study population and eligibility

During the study period, 160 women with advanced epithelial ovarian cancer were assessed for eligibility. Seven patients were excluded due to loss to follow-up before interval debulking surgery (n=3) or incomplete histopathological data required for Chemotherapy Response Score assessment (n=4). The final analytical cohort comprised 153 patients.

Eligible participants were women aged 18 years or older with FIGO 2014 stage III or IV epithelial ovarian cancer who received platinum-based neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) and had available post-surgical histopathological evaluation for chemotherapy response scoring. Patients were excluded if they had non-epithelial ovarian malignancy, did not receive NACT prior to surgery, had concurrent malignancies, or declined to participate.

### Pre-treatment evaluation and staging

Before initiation of NACT, all patients underwent standardized evaluation including clinical assessment, ECOG performance status, baseline serum CA-125, and contrast-enhanced computed tomography (CT) of the abdomen and pelvis for staging and operability assessment. Histopathological confirmation of epithelial ovarian carcinoma was obtained prior to chemotherapy initiation, using image-guided biopsy and or ascitic fluid cytology when clinically appropriate. Radiologic response during treatment was assessed on CT; RECIST version 1.1 criteria were applied when measurable disease was present.

### Neoadjuvant chemotherapy and surgical intervention

All patients received paclitaxel plus carboplatin administered every 21 days as platinum-based NACT. The number of cycles was determined by the treating gynecologic oncology team based on clinical response, radiologic assessment of resectability, and treatment tolerance. Interval debulking surgery was performed with the goal of complete macroscopic cytoreduction and typically included total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. Additional cytoreductive procedures, including peritonectomy, lymphadenectomy, bowel resection, or other organ resections, were undertaken as indicated by intraoperative disease distribution. Residual disease was categorized as no gross residual disease (R0) versus any gross residual disease (R1 or R2).

### Pathological evaluation and Chemotherapy Response Score

All resected specimens were processed according to routine institutional histopathology protocols. Chemotherapy Response Score (CRS) was assigned by consultant pathologists using the validated three-tier system for tumor regression following NACT: CRS 1 (minimal or no response), CRS 2 (partial response), and CRS 3 (complete or near-complete response). CRS was assessed on omental specimens and, where available, on adnexal specimens; for primary analyses, patients were grouped as CRS 1–2 versus CRS 3 to ensure adequate subgroup sizes. Pathologists were aware that patients had received NACT, and CRS assessment was not formally blinded to other clinical information; outcome data were not available at the time of specimen assessment.

### Data collection and outcome definitions

Clinical, treatment, and pathological variables were collected prospectively using a structured proforma, including age, FIGO stage, ECOG status, baseline CA-125, number of NACT cycles, radiologic response, CRS category, and residual

disease status. Follow-up evaluations were scheduled at 6 months, 12 months, and 36 months after IDS, and additionally as clinically indicated. Progression-free survival (PFS) was defined as the time from IDS to radiologic or clinical evidence of disease progression or death from any cause, whichever occurred first. Overall survival (OS) was defined as the time from IDS to death from any cause. Patients without an event were censored at the date of last contact. Platinum resistance was defined as disease progression or relapse within six months after completion of platinum-based chemotherapy.

### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0. Continuous variables are presented as mean  $\pm$  standard deviation and categorical variables as frequency and percentage.

Between-group comparisons (CRS 1–2 vs CRS 3) were conducted using independent-samples t-tests for continuous variables and chi square or Fisher’s exact tests for categorical variables, as appropriate. Survival curves for PFS and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. Binary outcomes at fixed timepoints, including progression and mortality at 6 months, 12 months, and 36 months, were explored using logistic regression, with results reported as odds ratios with 95% confidence intervals. Given subgroup size imbalance, regression models were kept parsimonious and estimates were interpreted cautiously. A two-sided p-value  $<0.05$  was considered statistically significant.

### Ethical considerations

Written informed consent was obtained from all participants prior to enrollment. Patient confidentiality was maintained by anonymizing study identifiers and restricting data access to the research team.

## 3. RESULTS

**Table 1: Baseline Clinicopathologic Characteristics and Treatment Exposure by Chemotherapy Response Score (CRS) (N = 153)**

Variable	CRS 1–2 (n = 126)	CRS 3 (n = 27)	p
<b>Age (years)</b>			
< 60	102 (81.0)	18 (66.7)	0.11
$\geq 60$	24 (19.0)	9 (33.3)	
Mean $\pm$ SD	49.5 $\pm$ 11.5	50.4 $\pm$ 8.9	0.71
<b>FIGO stage</b>			
Stage III	42 (33.3)	18 (66.7)	<b>0.002</b>
Stage IV	84 (66.7)	9 (33.3)	
<b>NACT cycles</b>			
2 cycles	6 (4.8)	3 (11.1)	0.18
3 cycles	75 (59.5)	15 (55.6)	
4 cycles	27 (21.4)	3 (11.1)	
5–6 cycles	18 (14.3)	6 (22.2)	

**Note:** Continuous variables compared using independent-samples t tests; categorical variables using chi-square tests.

Table 1 shows that the mean age was similar between groups, 49.5  $\pm$  11.5 years in CRS 1–2 versus 50.4  $\pm$  8.9 years in CRS 3 (p = 0.71). Most patients were younger than 60 years in both groups, 102/126 (81.0%) in CRS 1–2 and 18/27 (66.7%) in CRS 3, while age  $\geq 60$  years was 24/126 (19.0%) versus 9/27 (33.3%), respectively (p = 0.11). FIGO stage distribution differed between CRS categories, with Stage III comprising 42/126 (33.3%) in CRS 1–2 versus 18/27 (66.7%) in CRS 3, and Stage IV comprising 84/126 (66.7%) versus 9/27 (33.3%), respectively (p = 0.002). NACT cycle exposure was broadly comparable across CRS groups, with 3 cycles being most common, 75/126 (59.5%) in CRS 1–2 and 15/27 (55.6%) in CRS 3; the remaining distributions were 2 cycles 6/126 (4.8%) versus 3/27 (11.1%), 4 cycles 27/126 (21.4%) versus 3/27 (11.1%), and 5–6 cycles 18/126 (14.3%) versus 6/27 (22.2%) (p = 0.18).

**Table 2: Residual Disease Status After Interval Debulking Surgery by Chemotherapy Response Score (CRS) (N = 153)**

Residual disease status	CRS 1–2 (n = 126)	CRS 3 (n = 27)	<i>p</i>
No residual disease	45 (35.7)	24 (88.9)	< 0.001
Residual disease present	81 (64.3)	3 (11.1)	

*Note:* Values are presented as n (%). *p* value derived from Fisher’s exact test.

Table 2 demonstrates a marked difference in residual disease status after interval debulking surgery by CRS category. No gross residual disease was achieved in 45/126 (35.7%) of CRS 1–2 patients compared with 24/27 (88.9%) of CRS 3 patients, while residual disease remained present in 81/126 (64.3%) versus 3/27 (11.1%), respectively ( $p < 0.001$ ).

**Table 3: Long-Term Outcomes by Chemotherapy Response Score (N = 153)**

Outcome	CRS 1–2 (n = 126)	CRS 3 (n = 27)	<i>p</i>
Platinum resistance < 6 months	69 (54.8)	0 (0.0)	< 0.001
<b>Survival Status</b>			
Alive at 1 year	60 (47.6)	27 (100.0)	< 0.001
Alive at 3 years	34 (27.0)	21 (77.8)	< 0.001

*Note.* Values are presented as n (%). Platinum resistance was defined as disease progression or relapse within 6 months after completion of platinum-based chemotherapy. *p* value derived from fisher’s exact test for platinum resistance.

Table 3 shows that platinum resistance within 6 months occurred in 69/126 (54.8%) of patients in the CRS 1–2 group and in 0/27 (0.0%) of patients in the CRS 3 group ( $p < 0.001$ ). At 1 year, 60/126 (47.6%) of CRS 1–2 patients were alive compared with 27/27 (100.0%) of CRS 3 patients ( $p < 0.001$ ). At 3 years, survival remained lower in CRS 1–2, with 34/126 (27.0%) alive, versus 21/27 (77.8%) alive in CRS 3 ( $p < 0.001$ ).

**Table 4: Logistic Regression Analysis for Disease Progression at 1, 3, and 5 Years (N = 153)**

Variable	OR	95% CI	<i>p</i>
<b>Progression Within 1 Year</b>			
CRS 1–2 vs CRS 3	24.6	5.7–105.9	< 0.001
Residual disease present	5.2	2.2–12.3	< 0.001
<b>Progression Within 3 Years</b>			
CRS 1–2 vs CRS 3	11.8	3.8–36.5	< 0.001
Residual disease present	4.1	1.9–8.9	< 0.001

*Note:* OR = Odds Ratio; CI = Confidence Interval. Reference category is CRS 3. The Odds Ratio decreases over time (24.6 → 9.5) as the CRS 3 group eventually experiences late recurrences, but the association remains statistically highly significant.

Table 4 presents logistic regression results for disease progression at fixed timepoints, showing higher odds of progression among CRS 1–2 compared with CRS 3, and among those with residual disease present. For progression within 1 year, CRS 1–2 versus CRS 3 had an OR of 24.6 (95% CI 5.7–105.9,  $p < 0.001$ ), and residual disease present had an OR of 5.2 (95% CI 2.2–12.3,  $p < 0.001$ ). For progression within 3 years, CRS 1–2 versus CRS 3 had an OR of 11.8 (95% CI 3.8–36.5,  $p < 0.001$ ), and residual disease present had an OR of 4.1 (95% CI 1.9–8.9,  $p < 0.001$ ).

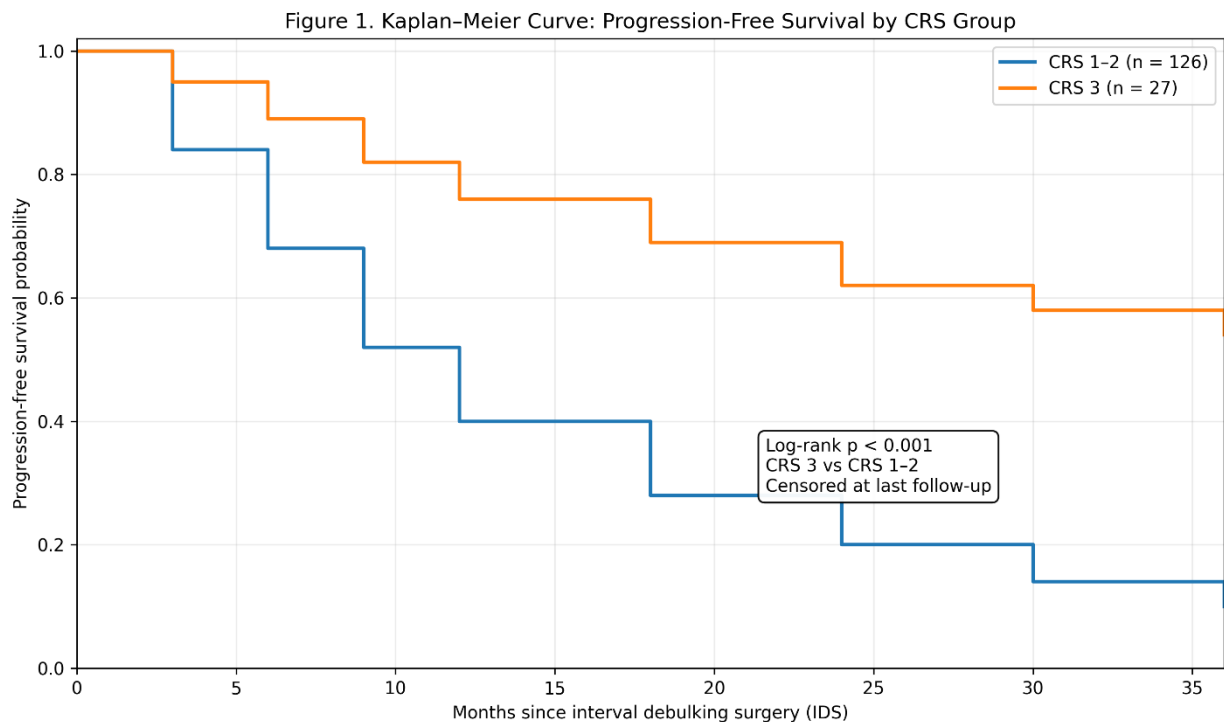
**Table 5: Univariable Logistic Regression Analysis for Survival at 1 and 3 (N = 153)**

Variable	OR	95% CI	<i>p</i>
<b>Survival at 3 Years</b>			
CRS 1–2 vs CRS 3	0.10	0.03–0.29	< 0.001
Age ≥ 60 years	0.95	0.52–1.73	.86
FIGO stage IV	1.42	0.78–2.60	.25

*Note:* OR = Odds Ratio; CI = Confidence Interval.

Table 5 shows that CRS category was strongly associated with 3-year survival on univariable analysis. Compared with CRS 3, CRS 1–2 had substantially lower odds of survival at 3 years (OR 0.10, 95% CI 0.03–0.29,  $p < 0.001$ ). In contrast,

age  $\geq 60$  years was not associated with 3-year survival (OR 0.95, 95% CI 0.52–1.73,  $p = 0.86$ ), and FIGO stage IV was also not associated with 3-year survival (OR 1.42, 95% CI 0.78–2.60,  $p = 0.25$ ).



**Figure 1: Kaplan-Meier Curve showing progression-free survival by CRS group.**

Figure 1 illustrates the Kaplan–Meier estimates of progression-free survival according to Chemotherapy Response Score category following interval debulking surgery. Patients with CRS 3 ( $n = 27$ ) demonstrated consistently higher progression-free survival probabilities across the follow-up period compared with those with CRS 1–2 ( $n = 126$ ). At approximately 12 months after surgery, the estimated progression-free survival was about 0.75 in the CRS 3 group compared with about 0.40 in the CRS 1–2 group. By around 24 months, progression-free survival remained higher in CRS 3 at approximately 0.62, whereas it declined to about 0.20 in CRS 1–2. The difference between the survival curves was statistically significant based on the log-rank test ( $p < 0.001$ ), with patients censored at their last follow-up time.

#### 4. DISCUSSION

In this prospective NICRH cohort of advanced epithelial ovarian cancer treated with paclitaxel–carboplatin NACT followed by IDS, most patients fell into CRS 1–2 (126/153), while CRS 3 constituted a smaller subgroup (27/153), a distribution pattern that aligns with multiple CRS validation cohorts where complete or near-complete histopathologic response is achieved in a minority of patients after NACT (12,13,15). Baseline age was comparable across CRS groups, both by categories ( $<60$  years: 81.0% vs 66.7%,  $p=0.11$ ) and by mean age ( $49.5 \pm 11.5$  vs  $50.4 \pm 8.9$  years,  $p=0.71$ ), supporting the view that CRS is primarily a tumor-response phenotype rather than a demographic surrogate (13,14). In contrast, stage distribution differed significantly, with CRS 3 being more frequent in FIGO stage III than stage IV (66.7% vs 33.3%,  $p=0.002$ ), a finding that is clinically plausible because lower metastatic burden may facilitate deeper histopathologic regression and more complete resection, although CRS studies often report heterogeneous relationships between stage and response due to NACT selection and restricted stage ranges (15,17). Treatment exposure by cycle number did not differ significantly ( $p=0.18$ ), suggesting that within real-world practice patterns, the depth of histopathologic regression was not simply a function of receiving more cycles, and this is consistent with reports where CRS stratification persists even when most patients receive similar NACT exposure (12,13). The most clinically actionable association in our dataset was the strong linkage between CRS and surgical cytoreduction: no gross residual disease (R0) was achieved in 88.9% of CRS 3 patients compared with 35.7% of CRS 1–2 patients ( $p<0.001$ ), while residual disease persisted in only 11.1% versus 64.3%, respectively (14,17). This pattern is concordant with prior work emphasizing that CRS tracks with operative endpoints and downstream prognosis, including studies that integrate both CRS and debulking status as complementary predictors, and cohorts showing that CRS retains prognostic signal even among completely

cytoreduced patients, indicating that CRS captures biology beyond what surgery alone can erase (17,18). Our early outcome signals were striking: platinum resistance within 6 months occurred in 54.8% of CRS 1–2 patients and in 0% of CRS 3 patients ( $p < 0.001$ ), and survival differed markedly at both 1 year (47.6% vs 100.0%,  $p < 0.001$ ) and 3 years (27.0% vs 77.8%,  $p < 0.001$ ), supporting a tight coupling between histopathologic regression and short to mid-term prognosis in this setting (12,15,19). The survival and progression analyses further reinforced this gradient, with CRS 1–2 associated with substantially higher odds of progression within 1 year (OR 24.6, 95% CI 5.7–105.9) and within 3 years (OR 11.8, 95% CI 3.8–36.5), and residual disease independently associated with progression at both timepoints (OR 5.2 and 4.1, both  $p < 0.001$ ), mirroring the broader literature where CRS and completeness of cytoreduction are repeatedly among the most influential prognostic variables after NACT–IDS (13,17,20). The Kaplan–Meier PFS curves also showed a clear separation by CRS group with log-rank  $p < 0.001$ , consistent with multiple open-access cohorts and pooled analyses demonstrating longer PFS in CRS 3 compared with CRS 1–2 across omental and adnexal scoring approaches (13,14,20). On univariable modelling of 3-year survival, CRS remained strongly associated (OR 0.10, 95% CI 0.03–0.29,  $p < 0.001$ ), whereas age  $\geq 60$  years ( $p = 0.86$ ) and FIGO stage IV ( $p = 0.25$ ) were not significant, a pattern that can occur in NACT-selected advanced-stage cohorts where CRS and residual disease dominate prognostic stratification, and where stage effects are attenuated by restricted stage range and treatment pathway homogeneity (17,21). Finally, emerging literature suggests that the strength of CRS prognostication may be modified in contemporary contexts by tumor genetics and post-frontline maintenance therapy, which may partly explain why effect sizes differ between cohorts and highlights the importance of interpreting CRS within local treatment realities, including access to maintenance strategies and the completeness and uniformity of follow-up (22,23).

#### **Limitations:**

This was a single-center cohort from a resource-limited setting, with marked CRS subgroup imbalance (CRS 3,  $n = 27$ ), so regression estimates, especially at fixed timepoints, may be imprecise and vulnerable to residual confounding. Pathologists were not formally blinded to clinical information, and the analysis did not incorporate key contemporary modifiers such as BRCA status, maintenance therapy exposure, or standardized post-IDS treatment variations, which may influence progression and survival patterns.

## **5. CONCLUSION**

In this NICRH cohort of advanced epithelial ovarian cancer treated with NACT followed by IDS, CRS was strongly associated with surgical outcome and early to mid-term prognosis. CRS 3 was linked to substantially higher complete macroscopic cytoreduction (R0, 88.9% vs 35.7%,  $p < 0.001$ ), absence of platinum resistance within 6 months (0.0% vs 54.8%,  $p < 0.001$ ), higher survival at 1 year (100.0% vs 47.6%,  $p < 0.001$ ) and 3 years (77.8% vs 27.0%,  $p < 0.001$ ), lower odds of progression within 1 year (CRS 1–2 vs CRS 3, OR 24.6, 95% CI 5.7–105.9,  $p < 0.001$ ) and 3 years (OR 11.8, 95% CI 3.8–36.5,  $p < 0.001$ ), and superior PFS by Kaplan–Meier analysis (log-rank  $p < 0.001$ ). These findings support CRS as a practical postoperative histopathologic marker for early risk stratification and outcome benchmarking after NACT–IDS in Bangladesh.

**Funding:** No funding sources.

**Conflict of interest:** None declared.

**Ethical approval:** The study was approved by the Ethics Committee of the National Institute of Cancer Research and Hospital, Dhaka, Bangladesh (Approval No. NICRH/Ethics/2021/263).

## **REFERENCES**

- [1] Tjokropawiro BA, Novitasari K, Ulhaq RA, Sulistya HA, Martini S. Investigation of the trends and associated factors of ovarian cancer in Indonesia: A systematic analysis of the Global Burden of Disease study 1990–2021. PLOS ONE. 2025 Jan 17;20(1):e0313418. doi:10.1371/journal.pone.0313418
- [2] Arnaoutoglou C, Dampala K, Anthoulakis C, Papanikolaou EG, Tentas I, Dragoutsos G, et al. Epithelial Ovarian Cancer: A Five-Year Review. Medicina (Kaunas). 2023 Jun 21;59(7):1183. doi:10.3390/medicina59071183 PubMed PMID: 37511995; PubMed Central PMCID: PMC10384230.
- [3] Arora T, Mullangi S, Vadakekut ES, Lekkala MR. Epithelial Ovarian Cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Dec 22]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK567760/> PubMed PMID: 33620837.

- [4] Medina-Franco H, Mejía-Fernández L. Neoadjuvant chemotherapy and interval debulking surgery for advanced ovarian cancer, an alternative with multiple advantages. *Chin Clin Oncol*. 2018 Dec;7(6):57. doi:10.21037/cco.2018.06.10 PubMed PMID: 30180749.
- [5] Coleridge SL, Bryant A, Lyons TJ, Goodall RJ, Kehoe S, Morrison J. Chemotherapy versus surgery for initial treatment in advanced ovarian epithelial cancer. *Cochrane Database Syst Rev*. 2019 Oct 31;2019(10):CD005343. doi:10.1002/14651858.CD005343.pub4 PubMed PMID: 31684686; PubMed Central PMCID: PMC6822157.
- [6] Nagao S, Tamura J, Shibutani T, Miwa M, Kato T, Shikama A, et al. Neoadjuvant chemotherapy followed by interval debulking surgery for advanced epithelial ovarian cancer: GOTIC-019 study. *Int J Clin Oncol*. 2023 Jun;28(6):804–15. doi:10.1007/s10147-023-02329-7 PubMed PMID: 37140771; PubMed Central PMCID: PMC10232639.
- [7] Xie Q, Cui M. The prognosis impact of NACT-IDS and PDS in advanced ovarian cancer: a systematic review and meta-analysis. *Journal of Gynecologic Oncology*. 2025 Apr 8;36(4). doi:10.3802/jgo.2025.36.e61
- [8] Qin M, Jin Y, Ma L, Zhang YY, Pan LY. The role of neoadjuvant chemotherapy followed by interval debulking surgery in advanced ovarian cancer: a systematic review and meta-analysis of randomized controlled trials and observational studies. *Oncotarget*. 2017 Dec 27;9(9):8614–28. doi:10.18632/oncotarget.23808 PubMed PMID: 29492221; PubMed Central PMCID: PMC5823572.
- [9] Charkhchi P, Cybulski C, Gronwald J, Wong FO, Narod SA, Akbari MR. CA125 and Ovarian Cancer: A Comprehensive Review. *Cancers (Basel)*. 2020 Dec 11;12(12):3730. doi:10.3390/cancers12123730 PubMed PMID: 33322519; PubMed Central PMCID: PMC7763876.
- [10] Chung YS, Kim HS, Lee JY, Kang WJ, Nam EJ, Kim S, et al. Early Assessment of Response to Neoadjuvant Chemotherapy with 18F-FDG-PET/CT in Patients with Advanced-Stage Ovarian Cancer. *Cancer Res Treat*. 2020 Oct;52(4):1211–8. doi:10.4143/crt.2019.506 PubMed PMID: 32599990; PubMed Central PMCID: PMC7577806.
- [11] Böhm S, Faruqi A, Said I, Lockley M, Brockbank E, Jeyarajah A, et al. Chemotherapy Response Score: Development and Validation of a System to Quantify Histopathologic Response to Neoadjuvant Chemotherapy in Tubo-Ovarian High-Grade Serous Carcinoma. *J Clin Oncol*. 2015 Aug;33(22):2457–63. doi:10.1200/JCO.2014.60.5212
- [12] Lawson BC, Euscher ED, Bassett RL, Liu J, Ramalingam P, Zhong Y, et al. A 3-Tier Chemotherapy Response Score for Ovarian/Fallopian Tube/Peritoneal High-grade Serous Carcinoma: Is it Clinically Relevant? *Am J Surg Pathol*. 2020 Feb;44(2):206–13. doi:10.1097/PAS.0000000000001391 PubMed PMID: 31651523; PubMed Central PMCID: PMC6954274.
- [13] Lee JY, Chung YS, Na K, Kim HM, Park CK, Nam EJ, et al. External validation of chemotherapy response score system for histopathological assessment of tumor regression after neoadjuvant chemotherapy in tubo-ovarian high-grade serous carcinoma. *J Gynecol Oncol*. 2017 Nov;28(6):e73. doi:10.3802/jgo.2017.28.e73 PubMed PMID: 28758379; PubMed Central PMCID: PMC5641524.
- [14] Santoro A, Angelico G, Piermattei A, Inzani F, Valente M, Arciuolo D, et al. Pathological Chemotherapy Response Score in Patients Affected by High Grade Serous Ovarian Carcinoma: The Prognostic Role of Omental and Ovarian Residual Disease. *Front Oncol*. 2019;9:778. doi:10.3389/fonc.2019.00778 PubMed PMID: 31482065; PubMed Central PMCID: PMC6709655.
- [15] Rodolakis I, Pergialiotis V, Lontos M, Haidopoulos D, Loutradis D, Rodolakis A, et al. Chemotherapy Response Score in Ovarian Cancer Patients: An Overview of Its Clinical Utility. *J Clin Med*. 2023 Mar 10;12(6):2155. doi:10.3390/jcm12062155 PubMed PMID: 36983157; PubMed Central PMCID: PMC10054535.
- [16] Manek S. The histological value of chemotherapy response score in advanced ovarian cancer—histopathological challenges. *Gynecology and Pelvic Medicine*. 2023 Jun 30;6(0). doi:10.21037/gpm-21-31
- [17] Zhong Y, Liu J, Li X, Westin SN, Malpica A, Lawson BC, et al. A Modified 2 Tier Chemotherapy Response Score (CRS) and Other Histopathologic Features for Predicting Outcomes of Patients with Advanced Extrauterine High-Grade Serous Carcinoma after Neoadjuvant Chemotherapy. *Cancers (Basel)*. 2021 Feb 9;13(4):704. doi:10.3390/cancers13040704 PubMed PMID: 33572451; PubMed Central PMCID: PMC7916221.
- [18] Santhamma AJ, Sambasivan S, Mohanan SC, Nair RP, J SR, James FV, et al. Prognostic Significance of Chemotherapy Response Score in Patients Undergoing Interval Debulking Surgery and Attained Complete Cytoreduction for High-Grade Serous Tubal and Ovarian Carcinoma. *South Asian J Cancer*. 2025 Jul;14(03):474–9. doi:10.1055/s-0044-1791834
- [19] Cohen PA, Powell A, Böhm S, Gilks CB, Stewart CJR, Meniawy TM, et al. Pathological chemotherapy response score is prognostic in tubo-ovarian high-grade serous carcinoma: A systematic review and meta-analysis of individual patient data. *Gynecologic Oncology*. 2019 Aug 1;154(2):441–8. doi:10.1016/j.ygyno.2019.04.679
- [20] Santoro A, Travaglino A, Inzani F, Straccia P, Arciuolo D, Valente M, et al. Prognostic Value of Chemotherapy Response Score (CRS) Assessed on the Adnexa in Ovarian High-Grade Serous Carcinoma: A Systematic Review and Meta-Analysis. *Diagnostics (Basel)*. 2022 Mar 4;12(3):633. doi:10.3390/diagnostics12030633 PubMed PMID: 35328186; PubMed Central PMCID: PMC8946962.
- [21] Lontos M, Andrikopoulou A, Koutsoukos K, Markellos C, Skafida E, Fiste O, et al. Neutrophil-to-lymphocyte ratio and chemotherapy response score as prognostic markers in ovarian cancer patients treated with neoadjuvant

- chemotherapy. *J Ovarian Res.* 2021 Nov 1;14:148. doi:10.1186/s13048-021-00902-0 PubMed PMID: 34724958; PubMed Central PMCID: PMC8561989.
- [22] Lee YJ, Shin YK, Kim NR, Kim SI, Lee YY, Park JY, et al. Chemotherapy response score no longer predicts survival outcomes in high-grade serous ovarian cancer patients with BRCA mutation and/or maintenance therapy. *Journal of Gynecologic Oncology.* 2024 Apr 22;35(6). doi:10.3802/jgo.2024.35.e73
- [23] Liang WF, Wang LJ, Li H, Liu CH, Wu MF, Li J. The added value of CA125 normalization before interval debulking surgery to the chemotherapy response score for the prognostication of ovarian cancer patients receiving neoadjuvant chemotherapy for advanced disease. *J Cancer.* 2021;12(3):946–53. doi:10.7150/jca.52711 PubMed PMID: 33403051; PubMed Central PMCID: PMC7778530.