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Research Article

A Study to Assess the Surgical Outcome in Patients of Advanced Epithelial Ovarian Carcinoma Undergoing Primary Debulking Surgery Versus Neoadjuvant Chemotherapy Followed by Interval Debulking Surgery

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Abstract

Objective: *Ovarian cancer is the third most common malignancy in Indian women, following breast and cervical cancers. Due to non-specific symptoms, diagnoses often occur at advanced stages. While primary surgery is the mainstay for early-stage disease, the best approach for advanced epithelial ovarian cancer remains debated.*

Methods: *This prospective observational study, conducted from January 2022 to December 2023, involved 60 patients with FIGO stage III and above. Patients were assigned to either primary debulking surgery (PDS, n=22) or neoadjuvant chemotherapy followed by interval debulking surgery (IDS, n=38). The aim was to compare optimal debulking rates between the two groups.*

Results: *Mean patient age was 53.5 years, with an average CA-125 level of 643.75. Optimal cytoreduction was achieved in both groups at similar rates (PDS: 86.4%, IDS: 89.5%). IDS showed a significant reduction in intra-operative bleeding (p=0.001), but experienced more post-chemotherapy toxicities (grades III and IV, p=0.021), and had a higher incidence of surgical site infection and wound breakdown. The most prevalent histology was high-grade serous carcinoma. Diaphragmatic carcinosis and mesenteric retraction emerged as independent predictors for suboptimal surgery. Compliance to treatment was marginally better in the IDS group. Disease-free survival at six months showed no major differences (PDS: 77.3%, IDS: 73.7%).*

Conclusion: *Though neoadjuvant chemotherapy reduced surgical blood loss and improved operability, it did not lead to significant survival benefits. The study supports personalized treatment strategies and calls for further research to optimize care in advanced ovarian cancer.*

Keywords: *Advanced Epithelial Ovarian Cancer, Primary Dsurgery, Interval Debulking Surgery, Neoadjuvant Chemotherapy, Cytoreductive Surgery, Stage III Ovarian Cancer*

Introduction

Ovarian cancer is the seventh most frequent cancer in women, affecting 324,603 people worldwide in 2022 (1). Most women with ovarian cancer are diagnosed at an advanced stage (2). Symptoms are frequently vague and brief, and no reliable screening programs are available. In early-stage disease (FIGO stage I / IIa), an aggressive surgery will cure the majority of women. The conventional treatment for advanced ovarian cancer (FIGO stage III/IV) is primary debulking surgery (PDS), followed by platinum-based therapy. The amount of tumor cytoreduction is regarded as the most important prognostic factor affecting survival.

Meta-analyses of non-randomised trials have now confirmed that survival is favourably correlated with the extent of tumor debulking (3,4). The definition of 'optimal' or 'maximal' debulking has altered since the 1980s. Originally viewed as no remaining tumor deposit of bigger than 2 cm in diameter, and more recently as residual tumor of ≤ 1 cm. The current goal is to leave no macroscopic disease.

NACT entails administering chemotherapy before cytoreductive surgery for advanced ovarian cancer. Bristow (2007) reviewed 26 non-randomized studies (NRS) comparing NACT to PDS and concluded that, while NACT may be a viable option for those who are unsuitable for primary cytoreduction due to factors like significant comorbidities, poor performance status, or surgical inoperability, survival outcomes with NACT may be inferior to PDS (3). Thus, platinum-based NACT could be an alternative to PDS, especially if complete cytoreduction is implausible upfront (5).

Tumour resectability is determined by the patient's age, tumor burden, co-morbidities, location of metastatic disease, performance status, and tumor stage. The goal of surgery, whether IDS or PDS, should be the complete removal of all tumor deposits (6). A study of 21 NRS revealed that, as compared to PDS, NACT increased the feasibility of optimum debulking (7). However, this does not appear to affect survival.

The use of NACT in advanced ovarian cancer has sparked significant debate in the literature (8). The US Society of Gynaecologic Oncology and the European Society of Gynaecologic Oncology report a significant disparity in acceptance and utilization of NACT as a therapy option for advanced ovarian cancer (5,9). Many researchers agree that NACT has a role, at least, in women with lesions that cannot be optimally resected, or in those who are not surgical candidates (3,8,10,11). Most of these studies showed that neoadjuvant chemotherapy provided no survival advantage (12–14). However, neoadjuvant chemotherapy improves surgical outcomes more than PDS (5). This study aims to evaluate the surgical outcome in patients of advanced epithelial ovarian cancer undergoing PDS and also in neoadjuvant chemotherapy followed by surgery.

Materials and Methods

Study Design:

The study was designed as an ambispective observational study evaluating effects of two treatment modalities which is "primary debulking surgery versus neoadjuvant chemotherapy followed by interval debulking surgery" in advanced epithelial carcinoma ovary with multiple endpoint variables.

Inclusion Criteria:

"Patients undergoing primary or interval debulking surgery for ovarian cancer" after getting approval from Multi-disciplinary Tumor Board with following:

a) Age between 18 to 70 years with biopsy/FNAC confirmed "stage III and IV epithelial ovarian cancer"

b) "Eastern Cooperative Oncology Group" (ECOG) performance status 0–2

c) Chemotherapy naïve patients

d) Women with duly signed written informed consent

e) "Adequate bone marrow function: White blood cells >3,000/μL, Absolute neutrophil count (ANC) ≥ 1.5 x 109/L, Platelet count ≥ 100 x 109/L"

f) "Renal function: Serum-Creatinine ≤ 1.5 x institutional upper limit normal (ULN), creatinine clearance ≥60 mL/min according to Cockroft-Gault formula"

g) "Hepatic function:

- Bilirubin ≤ 1.5 x ULN.
- SGOT ≤ 3 x ULN
- Alkaline phosphatase ≤ 2.5 x ULN"

Exclusion Criteria:

a) "Non-epithelial tumors" as well as "borderline tumors"; "low-grade carcinoma", "germ cell tumors"

b) Unresectable FIGO stage IV or with abdominal wall infiltration

c) History of synchronous or metachronous malignancy in the previous 5 years

d) Pregnant or breast-feeding female

e) Recurrent ovarian cancer

f) History of any prior abdominal/pelvic radiotherapy

g) Patients with dementia or altered mental status who could not have an understanding of giving an informed consent

Interventions:

The primary exposure variable was the type of treatment received ("primary debulking surgery or neoadjuvant chemotherapy followed by interval debulking surgery"). The specific chemotherapy regimens used were recorded.

Treatment given:

Surgery:

Patients either underwent upfront surgery (PDS) or were scheduled to undergo resection four weeks after having completed neoadjuvant treatment (IDS). Following surgeries were done:

Primary debulking surgery - Total Abdominal Hysterectomy with bilateral salpingo-oophorectomy with debulking of all visible disease (bulky pelvic and para-aortic lymphadenectomy, peritoneal stripping, liver capsule stripping, bowel resection and anastomosis - in case of infiltration, appendicectomy, total omentectomy).

Interval debulking surgery – The nature of debulking surgery was same as above, nomenclature changed as it followed neoadjuvant chemotherapy.

Based on the burden of residual disease post debulking surgery, further subclassified into:

"Complete Cytoreduction" – No visible residual disease

"Optimal Cytoreduction" – residual disease <1cm size

Sub-optimal Cytoreduction – residual disease >1cm size or gross disease

Chemotherapy:

The following chemotherapy regimen were administered in neoadjuvant chemotherapy arm and in adjuvant setting (Table 1).

Drugs	Dose	Days	Cycle	No. of Cycles
Paclitaxel + Carboplatin				
Paclitaxel	175 mg/ m^2	Day - 1	21 Days	3-4 Cycles
Carboplatin	AUC – 5			
Paclitaxel + Carboplatin +Bevacizumab				
Paclitaxel	175 mg/m^2	Day - 1	21 Days	3-4 Cycles
Carboplatin	AUC – 5			
Bevacizumab	15 mg/kg (omitted in last cycle)			
FOLFOX (mucinous)				
Oxaliplatin	85 mg/ m^2	Day - 1	21 days	3 Cycles
5-fluorouracil	400 mg/m^2 (bolus)			
Leucovorin	200mg/m^2			
5-fluorouracil	600 mg/m^2 (infusion)	48hrs		

Table 1 – Chemotherapy regimens and dosing frequency

Outcome Measures:

The primary outcome measure was rate of optimal debulking and secondary outcomes included short-term surgical outcomes like intraoperative blood loss, duration of ICU and hospital stay, postoperative complications (such as anastomotic leakage, infections, re-operation, 90-day mortality etc.), chemotherapy related toxicities and disease relapse within six months.

Sample Size Calculation:

The sample size was calculated for observational prospective comparative study, with an estimated outcome proportion of 0.47 (p1), 0.77 (p2) and precision level ± 5% with confidence interval 95%, Z score ~1.96 and using a desired power of 80% and a significance level of 0.05, a minimum sample size of 41 patients was required. (Figure 1)

$$n = \frac{Z^2 \cdot (p1 \cdot (1-p1) + p2 \cdot (1-p2))}{(p1-p2)^2}$$

Where:

- n = required sample size
- Z = Z-score corresponding to the desired level of confidence (e.g., for 95% confidence, Z ≈ 1.96)
- $p1$ = estimated proportion of the outcome in the control group
- $p2$ = estimated proportion of the outcome in the experimental group

Figure 1 – Formula used for sample size calculation

A total of 60 patients were included where Arm-A (Primary debulking surgery) had 18 patients and Arm-B (Interval debulking surgery) had 32 patients.

Data Collection:

The inclusion and exclusion criteria were cross-checked and validated. The complete pre-therapeutic work-up was done. Clinical tumor staging was made from CECT scan of the thorax, abdomen and pelvis. Written informed consent was taken from all patients before participating in the study. Data was collected from both from "electronic medical records", patients' case files, and prospectively maintained proforma. Parameters included patient demographics, tumor characteristics, treatment details, and clinical outcomes. Data was then entered into a secure electronic database and checked for accuracy and completeness.

Data Analysis:

Descriptive statistics were used to summarize the characteristics of the study population and the distribution of the outcome measures. The analysis includes logistic regression models to compare the perioperative mortality and postoperative complications between the two groups, as well as subgroup analyses to evaluate the effect of specific chemotherapy regimens on outcomes. Comparison of variables was performed using the $\chi 2$ (chi square) for categorical variables and the Student t test for continuous variables (where appropriate) and a significance observed at $p<0.05$. Multivariate subgroup analysis was performed using binomial logistic regression. All analyses adjusted for potential confounders such as age, sex, tumor stage, and comorbidities. A p-value of 0.05 or less was regarded as significant. SPSS software for windows 11 was used for the data analysis.

Assessments During Treatment Phase:

Treatment visits were done during neoadjuvant chemotherapy including measurements of patients' vitals, weight and routine blood tests, nutritional status was recorded. Preoperatively clinical re-staging of the tumor

was carried out, within 4 weeks after end of neoadjuvant treatment by CECT scan of the thorax and abdomen, PET-CT, echocardiography and staging laparoscopy (in selected cases).

Follow-up of patients:

Post definitive treatment in either arm (primary or interval debulking surgery) patient was discharged and asked to visit the hospital after 10-14 days for first follow-up and subsequently after 2 weeks interval. After availability of final histopathological report, patient was sent to medical oncology department for adjuvant systemic treatment as per the pathological stage and histology. Patients were regularly evaluated and noted for any systemic toxicity during each cycle of chemotherapy (grouped and classified as per CTCAE v5.0) and thereafter patient was followed up in surgical oncology out-patient department at 2-3 months interval up to a period of 6 months.

Ethical Issues:

Prior to the commencement, ethical clearance was obtained from the **Ethical & Scientific Committee of Srimanta Sankaradeva University of Health Sciences, Guwahati, Assam with Approval no (MC/190/2007/Pt-II/Oct.2022/27).**

Informed Consent:

Eligible patients were briefly explained about the nature of study and a written informed consent was obtained.

Results

The mean age in PDS group was 46.04 $\pm$ 11.40 years and IDS was 53.5 $\pm$ 8.73 years. For subgroup analysis, age was further subclassified into young (<50yrs) and old ($\geq$50yrs). Majority of patients who underwent upfront surgery were young (59.1%) compared to NACT group (36.8%). Majority patients were multiparous (78.33%), 7 were uniparous (11.67%) and 4 were nulliparous. Among the multiparous female, mean parity was 2.70 (range: 2 to 7). Surprisingly, there was no history of oral contraceptive intake in any of the patients. Most common presentation was pain abdomen (58.34%), abdominal distension (51.67%), anorexia (21.67%), generalized weakness (30%), lump in abdomen (13.34%). Other uncommon symptoms like per vaginal bleed, breast mass, shortness of breath, abdominal discomfort and loss of weight in 8% patients. Only ECOG 1 and 2 were part of this study. In the PDS group, majority of patients had ECOG 1 (95.5%) while IDS group had more ECOG 2 patients (15.8%).

Out of 60 patients, 34 patients had ascites (56.7%). Looking at the group distribution, 9 patients in PDS arm (40.9%) and 25 patients in IDS arm (65.8%) had presence of ascites on clinical examination. However, it was

not statistically significant (p-value: 0.061). The distribution of body weight was comparable in both groups (p-value: 0.97). Mean and Standard deviation of body weight was 49.50 + 12.21 and 49.43 + 7.10 in PDS and IDS group respectively. Mean CA-125 level for the entire subset was 643.75. Further subgroup analysis was done in both treatment arms, mean levels were 474.70 and 741.61 in PDS and IDS arm respectively. When tested for significance, the level was found to be comparable in both groups (p-value: 0.205).

Table 2 - SUMMARY OF PATIENT DEMOGRAPHICS			
Patient Characteristics	**PDS (n=22)**	**IDS (n= 38)**	**P value**
Age (years) mean ± SD	46.04 ± 11.40	53.50 ± 8.73	0.095
Marital status			
Yes	21 (95.4%)	38 (100%)	
No	1 (4.54%)	-	
Co-morbidity			
Yes	3 (13.63%)	12 (31.75%)	
No	19 (86.36%)	26 (68.42%)	
Past surgical history			
Yes	8 (36.36%)	12 (31.75%)	
No	14 (63.64%)	26 (68.42%)	
Menopausal status			
Premenopausal	11 (50%)	7 (18.42%)	
Perimenopausal	3 (13.63%)	3 (7.90%)	
Postmenopausal	8 (36.36%)	28 (73.68%)	
OCP Intake	-	-	
Family History	1	-	
Mean Parity	2.27	2.04	
Clinical presentation			
Pain abdomen	12 (54.54%)	23 (60.52%)	
Abdominal distension	8 (36.36%)	23 (60.52%)	
Anorexia	3 (13.63%)	11 (28.94%)	
Generalized weakness	6 (27.27%)	12 (31.57%)	
Abdominal lump	4 (18.18%)	4 (10.52%)	
Others	2 (9.09%)	3 (7.89%)	
Performance status			

ECOG 1	21 (95.4%)	32 (84.21%)	
ECOG 2	1 (4.54%)	6 (15.79%)	
Mean Body weight (Kg)	49.50 ± 12.21	49.43 ± 7.10	0.978
Ascites	9 (40.90%)	25 (65.78%)	0.061
CA – 125 level (mean)	474.70	741.61	0.205

Table 2: Summary of patient demographics, [PDS – Primary debulking surgery; IDS – Interval debulking surgery; OCP – Oral contraceptive pill; ECOG – Eastern Cooperative Oncology Group]

Cross-sectional imaging (Contrast enhanced CT / MRI) was done for every patient for assessing the tumor burden and following points were specially noted: "presence of peritoneal carcinosis, omental caking/ nodularity, diaphragmatic carcinosis, mesenteric retraction, bowel infiltration, stomach infiltration and liver metastasis" (Figure 2).

Overall in the study population, 81.7% had peritoneal dissemination. In the PDS group, 15 patients (68.2%) had peritoneal disease while 34 patients (89.5%) in the IDS group. Fifty-two out of 60 study subjects (86.7%) had presence of omental caking/nodularity. In the PDS group, 17 patients (77.3%) and 35 patients (92.1%) in the IDS group had omental involvement. Overall, 15% of patients had disease involvement of either hemi-diaphragm. On subgroup analysis, only 1 (4.5%) patient had diaphragmatic carcinosis in PDS arm while 8 (21.1%) of them were involved in IDS arm, and statistically not significant. Around 6.7% patients had mesenteric retraction, out of which PDS group had only 1 patient and IDS had 3 patients. About 26.7% (16 out of 60) of the total patients had bowel infiltration on imaging which required bowel resection. In the PDS arm, 6 patients (27.3%) had bowel infiltration and 10 patients (26.3%) in the IDS group. None of the patients had stomach infiltration. A total of 2 patients had liver metastases and both underwent NACT followed by IDS.

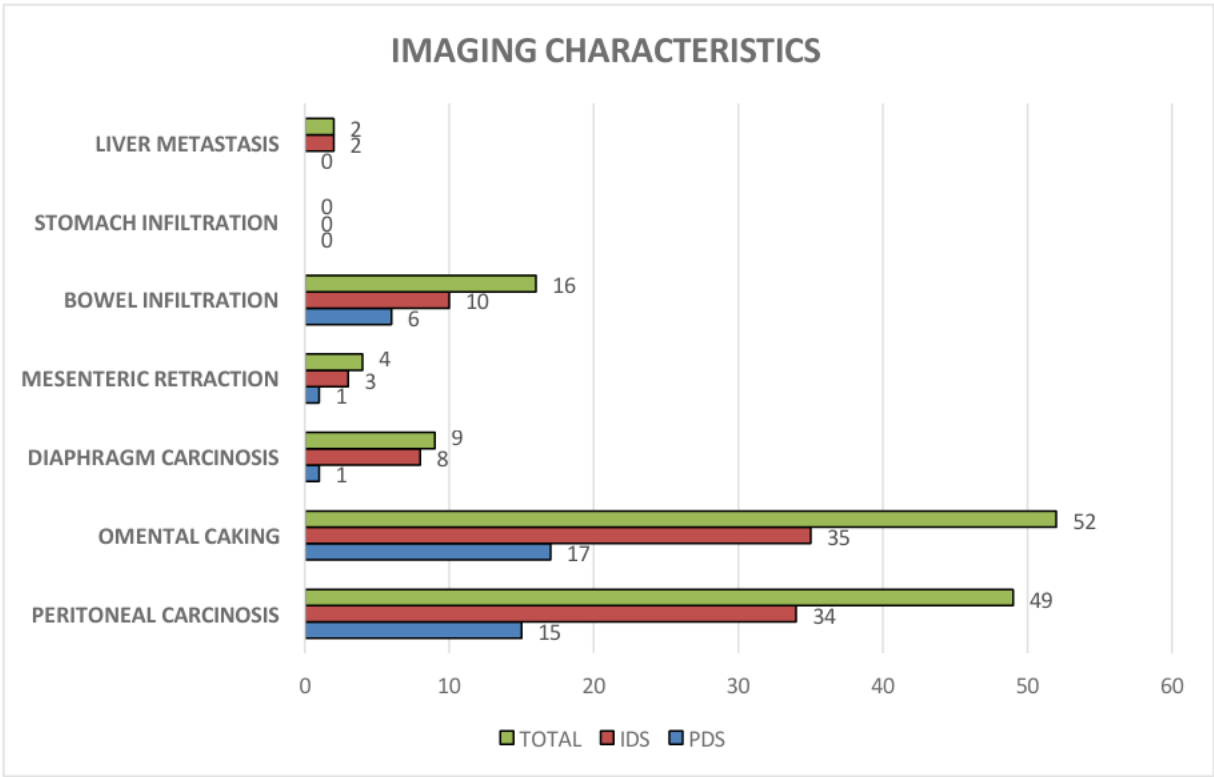

Figure 2: Imaging Characteristics of the study population, [IDS – Interval debulking surgery; PDS – Primary debulking surgery]

Intraoperative Outcomes

TYPE OF SURGICAL DEBULKING: This group was subdivided into optimal debulking and sub-optimal debulking based on the residual tumor burden. Overall, 53 patients out of 60 (88.3%) had complete debulking. On subgroup analysis, the optimal debulking rate was comparable in both groups (86.4% vs 89.5%; PDS vs IDS) with a p-value of 0.718 (chi-square test) (Figure 3). On binomial logistic regression analysis, diaphragmatic carcinosis (p-value: 0.028) and mesenteric retraction (p-value: 0.013) were two independent factors associated with sub-optimal debulking (Table 3).

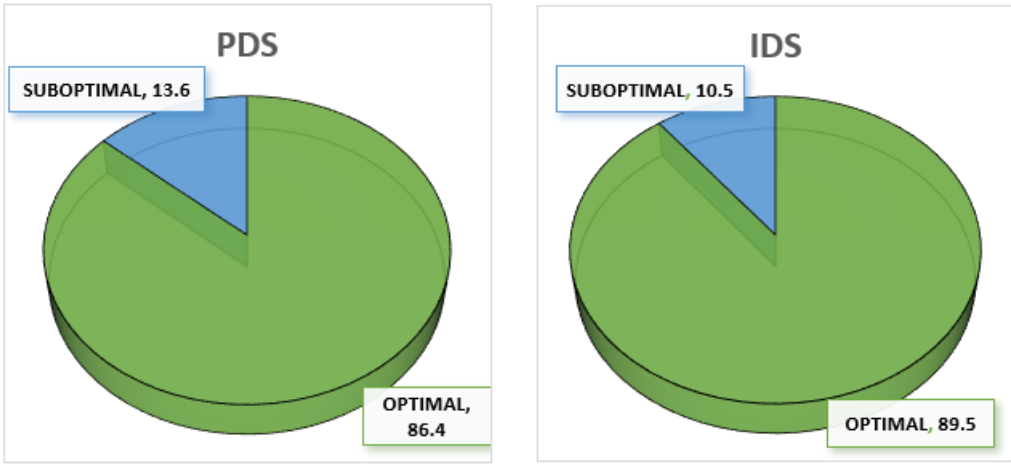

Figure 3 – Intraoperative Outcome (Rate of Debulking: optimal vs suboptimal); [PDS – Primary debulking surgery; IDS – Interval debulking surgery]

Variables	Total	Optimal (N=53)	Suboptimal (N=7)	Odds Ratio	Lower	Upper	P value
Age >50 yrs	33	30	3	0.54	0.106	2.768	.462
Ascites	34	30	4	1.09	0.214	5.591	.913
CA 125>500	31	27	4	1.41	0.276	7.198	.680
Peritoneal Carcinosis	49	43	6	2.91	0.242	35.122	.399
Omental caking	52	45	7	0			1
Diaphragm carcinosis	9	6	3	**0.17**	0.028	1.058	**0.028***
Mesenteric Retraction	4	2	2	**0.11**	0.011	1.193	**0.013***
Bowel infiltration	16	13	3	0.72	0.112	4.676	0.735
Liver Metastasis	2	1	1	0.03	0.001	1.263	0.067
Neoadjuvant Chemotherapy	38	34	4	0.965	0.791	1.17	0.176
Bowel Resection	18	16	2	1.84	0.173	19.662	0.611
CTCAE Grade 3/4	33	28	5	1.61	0.833	3.315	0.150
Stage IV	6	5	1	0.53	0.051	5.503	0.596

Table 3 - Binomial Logistic regression for factors associated with Optimal Debulking; [CTCAE – Common Terminology Criteria for Adverse Events]

The mean intra-operative blood loss was 305.33 ml (Table 4). In the PDS group mean blood loss was significantly greater than IDS group (334.54 ± 33.05 vs 288.42 ± 41.49; p-value: <0.001, independent t-test)

Variable	Grp PDS (N=22)		Grp IDS (N=38)		P value
	Mean	SD	Mean	SD	
Operating time	303.18	35.10	286.84	27.71	0.069
Blood loss	334.54	33.05	288.42	41.49	**<0.001****

Table 4 - Mean Operating time and blood loss in both groups, [IDS – Interval debulking surgery; PDS – Primary debulking surgery] "Independent t test; **p<0.001 highly significant"

Post-Operative Outcomes

A total of 18.3% patients developed SSI after surgery. The proportion of patients with SSI was higher in IDS group than PDS (23.7% vs 9.1%), however not statistically significant (p-value: 0.159). Only 3 patients developed sheath dehiscence in the total population, all had undergone neoadjuvant chemotherapy followed by IDS. However, no statistical significance was found between the two groups. None of the patients developed any anastomotic leak or fistula in the post-operative period. There was no instance of relaparotomy for any of the surgery related complication in the entire population. Mean ICU stay overall was 2.28 days (ranging from 1 to 7 days). Only 1 patient had a stay of 7 days with suboptimal resection, belonging to IDS group. Comparison of the mean between PDS and IDS group was not statistically significant (p-value: 0.322). Mean duration of stay in the hospital was 8.38 days (ranging from 4 – 34 days). Mean hospital stay was comparable between two groups (8.04 ± 2.83 vs 8.57 ± 4.94; PDS vs IDS). There were no 90-day mortality in the entire study population.

The chemotherapy related toxicity was graded as per CTCAE v5.0 and were grouped into different systems like hematological, gastro-intestinal, genito-urinary, skin and neurological. Overall, 33 patients (55%) developed some form of adverse events which were ≥ grade 3 as per CTCAE v 5.0. Only 1 patient developed grade 4 complication in the IDS group (Table 5). Most common complication were haematological (myelosuppression) and were managed by administration of GM-CSF injections, deferring next cycle of chemotherapy for a few days till the absolute neutrophil count recovered. The rate of complications was higher in the group receiving neo-adjuvant chemotherapy (IDS group) compared to the upfront surgery group (68.42% vs 31.8%; p-value: 0.021).

CTCAE	Grp PDS		Grp IDS		Total		P value
	N=22	%	N=38	%	N=60	%	
None	15	68.2	12	31.6	27	45.0	**0.021***
Grade 3	7	31.8	25	65.8	32	53.3	
Grade 4	0	0.0	1	2.6	1	1.7	

Table 5 - Chemotherapy related toxicities in both groups, [IDS – Interval debulking surgery; PDS – Primary debulking surgery] "*Chi square test; p>0.05 not significant"

Compliance to Treatment: Overall, 88.3% patients completed the entire course of treatment and the proportion was comparable in both treatment groups (81.8% vs 92.1%; PDS vs IDS). Most common histology was "High grade serous carcinoma" (HGSC) in 80% of patients followed by mucinous adenocarcinoma (8.3%) and clear cell carcinoma (3.3%). Most common stage on histopathology report was stage IIIB (Figure 4). At 6 months follow-up, disease relapse rate was 9.1% in PDS group and 13.2% in IDS group. However, there was no statistical difference between the groups.

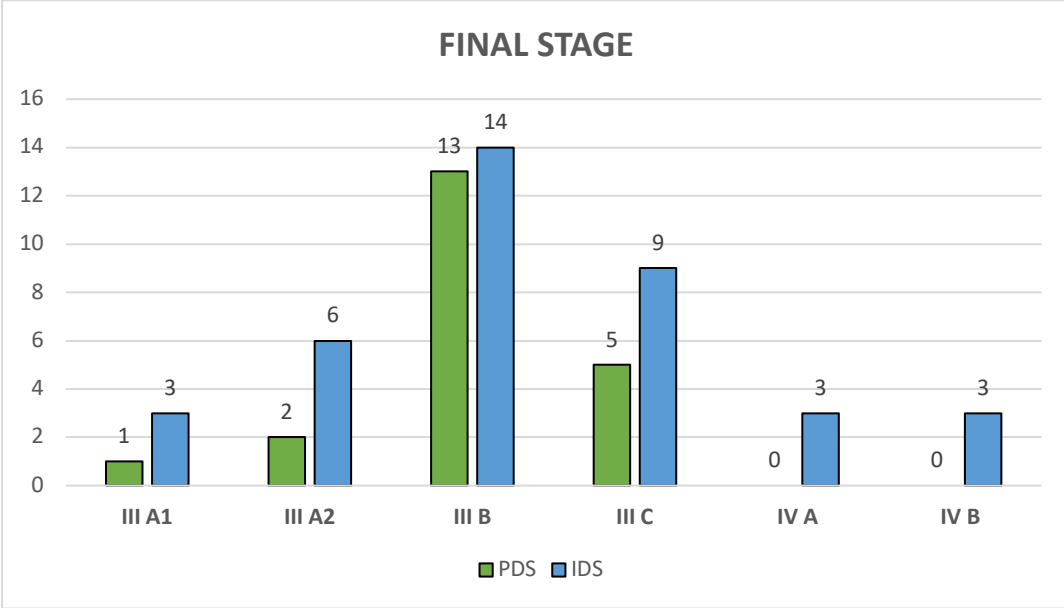

Figure 4 – Stage Distribution of patients in both groups, [IDS – Interval debulking surgery; PDS – Primary debulking surgery]

Discussion

To date, there is no objective consensus on the superiority of neoadjuvant therapy to upfront debulking surgery as a "standard of care" in patients with "locally advanced ovarian cancer". Recent guidelines like NCCN, ESMO, and ESGO advocate the use of NACT in patients with high-burden disease, poor performance status, and in those unfit for surgery (15–17). However, there is no documented benefit in overall or progression-free survival with the use of NACT. There is evidence to suggest that NACT is non-inferior to upfront surgery in terms of disease control and provides better chances at optimal debulking of tumors in advanced ovarian cancer. Therefore, many RCTs are being pursued between NACT and primary debulking surgery, and a few years from now, the results will be clearer.

The analysis of our dataset revealed that the patients in both groups had similar characteristics in terms of age distribution, marital status, presence of co-morbidity, menstrual status, parity, and past surgical history. On cross-sectional imaging during the initial staging workup, diffuse peritoneal carcinosis was significantly more in the IDS subset (89.5% vs 68.2%; p-value: 0.04).

In our study, the rate of optimal debulking was 86.4% in the PDS group and 89.5% in IDS group, with p-value: 0.718. This suggests that the chances of optimal debulking is slightly improved with neoadjuvant chemotherapy, but the difference is not statistically significant. Large RCTs like the EORTC 55791, CHORUS, JCOG 0602, SCORPION have in the past suggested an improved rate of optimal surgical debulking with the use of neoadjuvant chemotherapy (5,12,18,19). EORTC 55791 study documented that complete cytoreduction was performed in 19.4% in PDS and 51.2% in IDS group (5). CHORUS trial had 39% complete cytoreduction in IDS group compared to 17% in PDS group (19). Similarly, JCOG 0602 62% complete debulking rate in IDS group versus 12% in the PDS group (18) SCORPION trial also had superior rates of optimal debulking with neoadjuvant chemotherapy (67% vs 47.6%) compared to upfront surgery (12). There is a striking difference is outcome when compared with previous literature (Table 6).

Apparently, in our study, it seems that the rate of debulking is not affected with the use of neoadjuvant chemotherapy and that the rate of complete debulking is similar. However, it is noticed that most of the patients in the IDS group had significantly more tumor burden on imaging compared to those in PDS group (although no statistical difference was found). The percentage of patients with peritoneal, diaphragmatic carcinosis, and bowel and liver metastasis were almost double in IDS subset. Despite this difference, the rates of optimal debulking was similar which emphasizes the benefit of neoadjuvant treatment in our study. Binomial logistic regression analysis revealed the presence of diaphragmatic carcinosis and mesenteric retraction to be independent factors associated with sub-optimal debulking. Overall, the results of this study suggest that there is no significant difference in post-operative outcomes between patients who received NACT and patients who underwent upfront surgery.

However, due to observational nature of the study and unanimous role of institutional tumor board in treatment selection, there was significant selection bias. This also reflects in the outcome of the study.

Parameters (values in %)	**EORTC 55791**(5) **(n = 718)**		**CHORUS**(5) **(n = 552)**		**JCOG 0602**(18) **(n = 301)**		**SCORPION**(12) **(n = 280)**		**Our Study (n = 60)**	
	PDS	IDS	PDS	IDS	PDS	IDS	PDS	IDS	PDS	IDS
Optimal Debulking	19.4	51.2	15	36	31	55	45.5	57.7	86.4	89.3
Bowel resection	15.4	8.69	10.5	8.2	37.6	23.7	41.8	7.70	31.8	28.9
Blood transfusion	58.3	53.6	NA	NA	66.6	52.6	27.2	9.6	90	96.2
SSIs	8.1	1.7	6	3	0.7	0.8	7.27	0	9.1	23.7
Chemotherapy toxicity	NA	NA	49	40	20.3	18	22.6	7.6	31.8	68.4
Perioperative mortality	2.5	0.7	6	<1	0.7	0	1.7	0	0	0

Table 6 – Comparison of outcomes with available literature (RCTs); [IDS – Interval debulking surgery; PDS – Primary debulking surgery]

Our study demonstrates that the addition of neoadjuvant chemotherapy leads to less intra-operative blood loss, but, at the cost of more risk of post-operative complications and chemotherapy related grade 3 and 4 toxicities. The compliance to treatment and percentage of patients completing treatment was slightly better in PDS arm. These findings support the potential clinical benefit of combining neoadjuvant chemotherapy with standard surgery in specific patient population. However, the impact on post-operative outcomes and complications remains inconclusive. A clear advantage of IDS over PDS has not been established and the study was not intended from the beginning to look for differences in survival. Being a strict time bound study as a part of

academic thesis, longer followup to evaluate survival outcomes could not be performed.

In conclusion, our study provides valuable insights into the comparative effectiveness of neoadjuvant chemotherapy versus upfront debulking surgery in patients with advanced epithelial ovarian cancer. It is evident that major response to preoperative treatment is an important prognostic factor, and future trials should aim to optimize preoperative treatment by combining all treatment modalities, including chemotherapy, targeted therapy, and novel molecular targets. Ultimately, a multidisciplinary approach considering individual patient characteristics and long-term outcomes assessment will be crucial in determining the optimal treatment approach for these patients.

Conflict of Interest: None

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