**Original Research Article**

# Effect of neoadjuvant chemotherapy in advanced ovarian carcinoma

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## Abstract

**Background:** Ovarian cancer is the second most common gynecological malignancy. Patients with ovarian tumors are often asymptomatic for a long time. Most cases are diagnosed late because effective screening methods are not available.

**Aim of the study:** The tumor clearance effect of neoadjuvant chemotherapy in the advanced ovarian tumor in terms of optimal debulking, ascitic fluid volume reduction, blood transfusion requirements and to compare it with those who have not received neoadjuvant chemotherapy.

**Materials and methods:** 25 Patients with advanced ovarian tumor admitted in the Institute of Obstetrics and Gynecology, ISOKGH, Chennai from February 2018 to December 2018 were included in the study. All patients enrolled in the study underwent a detailed physical examination, routine hematological, biochemical investigations, Ultrasound, and CT Scan. For those patients with ascites, ascitic fluid was sent for cytology. When cytology report confirmed that it was Epithelial ovarian tumor, the patient received Neoadjuvant chemotherapy of Cisplatin 75mg/sq. m, Cyclophosphamide 750 mg/sq. m for 3 cycles – 6 weeks.

**Results:** In our study, injury to adjacent structures was present in 7 cases of PDS group (28%) whereas 3 cases in NACT had an injury. Out of the total 10 cases, 2 had bladder injury, 2 had an injury to the small bowel, 3 had a ureteric injury, 2 had a sigmoid colon and the other had a rectal injury. Post-op complications were present in 8 cases of PDS group (32%), 4 cases (16%) of NACT/IDS group in our study.

**Conclusion:** Neoadjuvant chemotherapy is significantly more effective in achieving optimal cytoreduction and reducing the ascitic fluid volume in advanced ovarian cancer. Blood transfusion requirement is significantly less in the neoadjuvant chemotherapy group.

**Key words**

Blood transfusion, Chemotherapy, Ovarian Carcinoma, Ascites.

## Introduction

Overall, Ovarian cancers account for 5% of all cancer diagnosis. The lifetime risk of developing ovarian cancer is approximately 1.4-1.9%. Epithelial ovarian cancer is a disease of the older women mean age at diagnosis being 60 but it can occur at any age. About 40% of EOCs occur at>70 years of age and 70% are at stage 3 or 4 at diagnosis [1]. The incidence in developing countries is 9.4/100,000. In India, ovarian cancer rank 6th most common cancer in women [2]. The overall survival rate is about 20%. The risk of developing ovarian cancer increases as age increases. Ovarian cancer is rare in women younger than 40. Most ovarian cancers are postmenopausal. 50% of all ovarian cancers are found in women for more than 60 years. Obesity increases the risk of developing many cancers [3]. Obese women with a body mass index (BMI) of more than 30 may have a higher risk of developing ovarian cancer. Obesity may also affect the overall prognosis of a woman with ovarian cancer [4]. Women who have their first full-term pregnancy after age 35 or who never carried a pregnancy to term have a higher risk of ovarian cancer [5]. The risk of some other cancers, such as pancreatic cancer and prostate cancer, are also increased. Mutations in BRCA1 and BRCA2 are also responsible for most inherited ovarian cancer. The lifetime risk of developing ovarian cancer for women with a BRCA1 mutation is estimated to be between 35% -40% [6]. For women with BRCA2 mutations, the risk has been estimated to be between 13%-23%. In comparison, the lifetime risk of developing ovarian cancer for women in the general population is less than 2%. BRCA 1 associated cancer occurs earlier. BRCA 2 have a better prognosis. PTEN tumor hamartoma syndrome also known as Cowden disease, people are primarily affected with thyroid problems, thyroid cancer, and breast cancer. Women also have an increased risk of endometrial and ovarian cancer. It is caused by inherited mutations in the PTEN gene [7]. Women with this syndrome have a very high risk of colon cancer and also have an increased risk of developing endometrial cancer and ovarian cancer. Many different genes can cause this syndrome. They include MLH1, MLH3, MSH2, MSH6, TGFBR2, PMS1, and PMS2. The lifetime risk of ovarian cancer in women with hereditary nonpolyposis colon cancer (HNPCC) is about 10%. Up to 1% of all ovarian epithelial cancers occur in women with this syndrome. Another name for HNPCC is Lynch syndrome [8].

## Materials and methods

25 Patients with advanced ovarian tumor admitted in the Institute of Obstetrics and Gynecology, ISOKGH, Chennai-February 2018 to Dec 2018 were included in the study. All patients enrolled in the study underwent a detailed physical examination, routine hematological, biochemical investigations, Ultrasound, and CT Scan. For those patients with ascites, ascitic fluid was sent for cytology. When Cytology report confirmed that it was Epithelial ovarian tumor, the patient received Neoadjuvant chemotherapy of Cisplatin 75 mg/sq. m, Cyclophosphamide 750 mg/sq. m for 3 cycles – 6 weeks.

**Inclusion criteria**

- Patients with advanced epithelial ovarian tumor (stage 3 and 4).
- No previous Chemotherapy.
- No Previous Surgery for the same complaint.
- Willing to take neoadjuvant Chemotherapy and then follow it up with surgery.

**Exclusion criteria**

- Early stage epithelial ovarian tumor (Stage 1 and 2).
- Borderline tumor.

- Those who were treated with some form of Oncotherapy.
- Not willing to wait for surgery following CT.

Optimal Debulking, Ascitic fluid volume, Blood transfusion rate were compared with the control group. Control group in this study was those patients with advanced epithelial tumor who had not received neoadjuvant chemotherapy and undergone primary cytoreductive surgery.

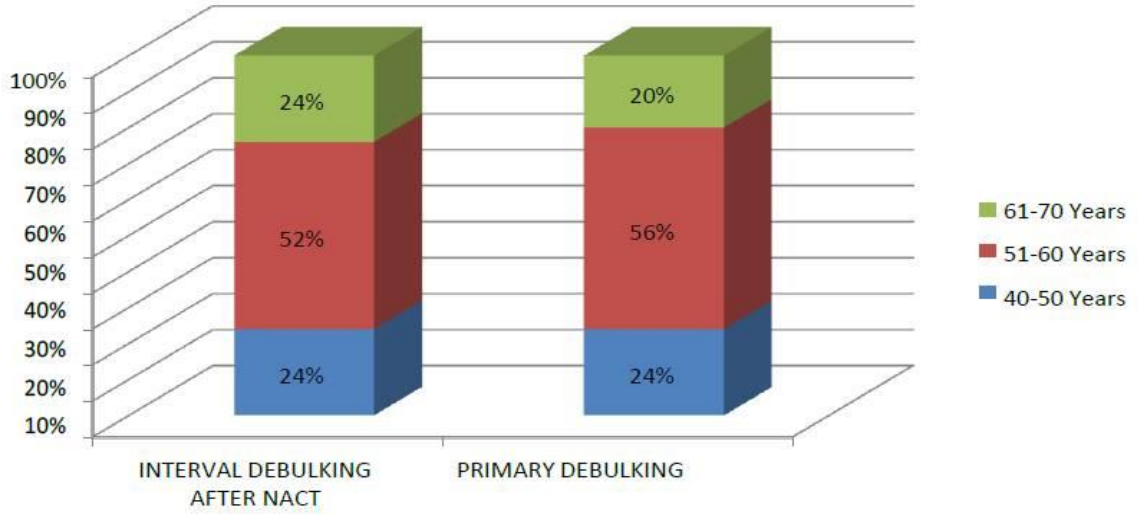
**Statistical analysis**

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS) Version 17.0. Chicago: SPSS Inc.). Continuous variables were presented as a mean ± standard deviation, and categorical variables were presented as absolute numbers and percentage. Data were checked for normality before statistical analysis using a Shapiro-Wilk test. Normally distributed continuous variables were compared using ANOVA.

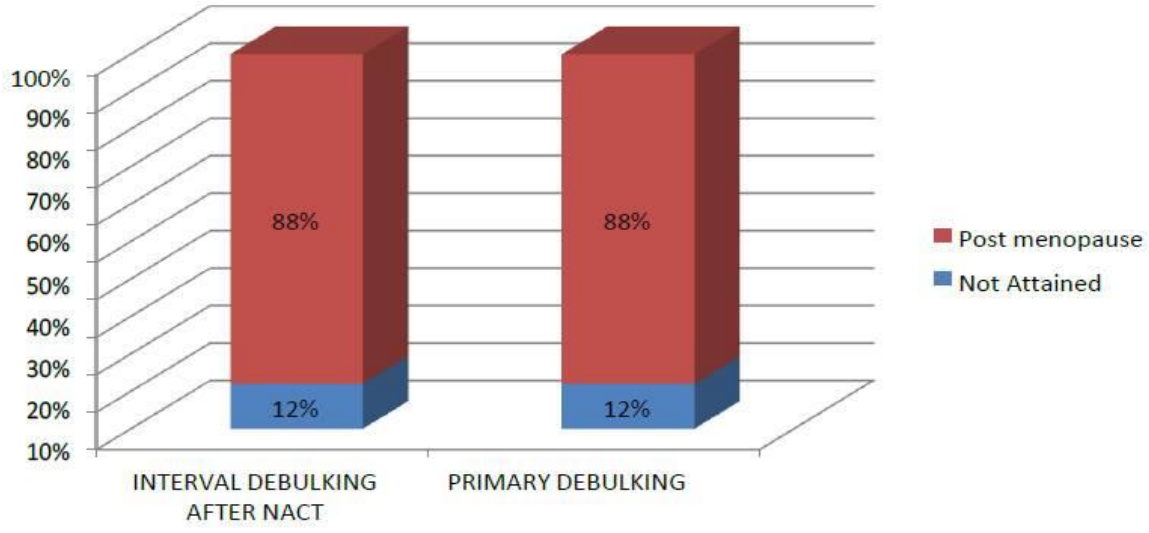
## Results

**Graph - 1** shows in our study the range of age was from 40 to 70 years with a median age of 55 years. The range was 52-73 years.

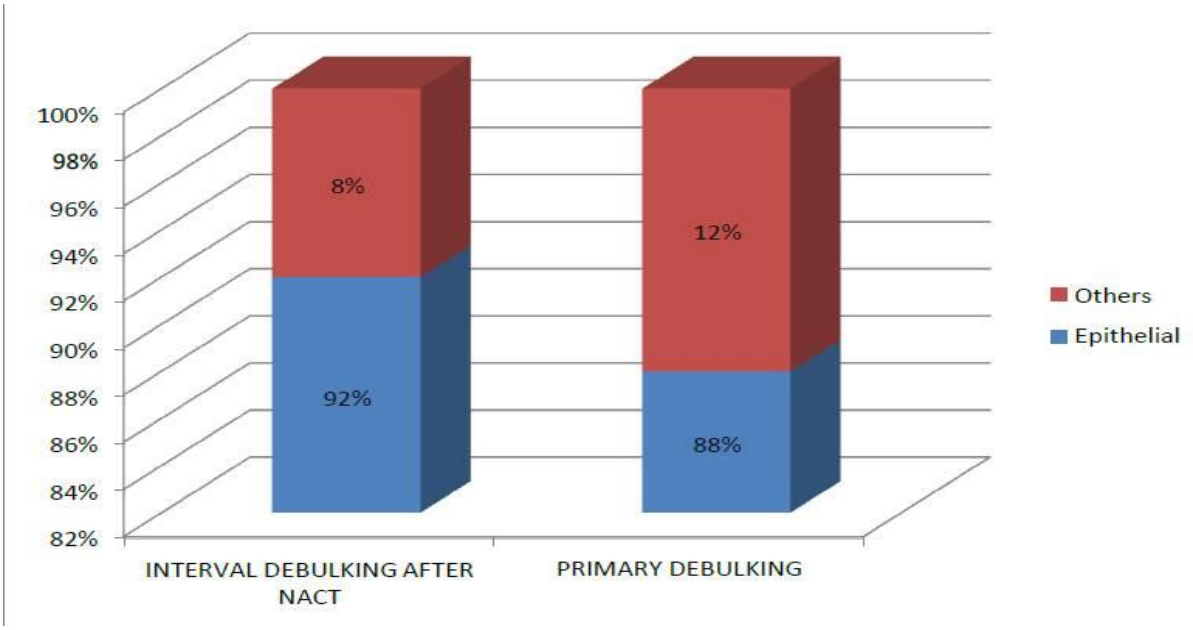
**Graph – 1:** Age distribution.



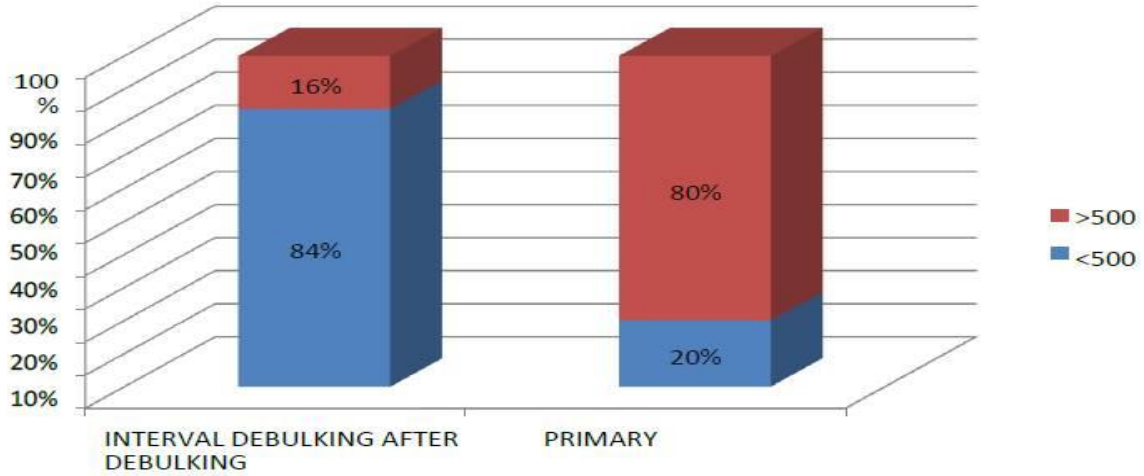

**Graph – 2:** Menopausal status.



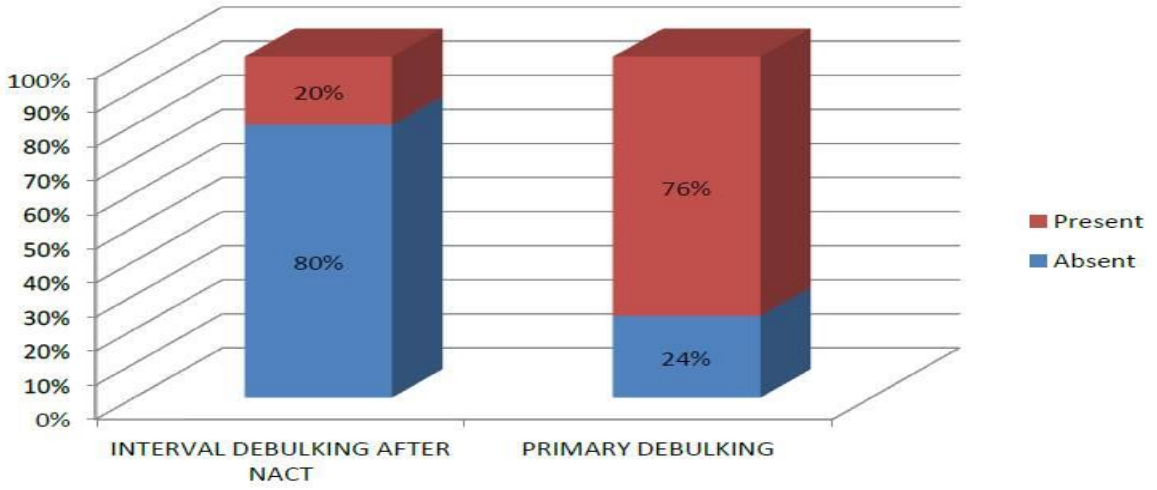
**Graph – 3:** Histological diagnosis.



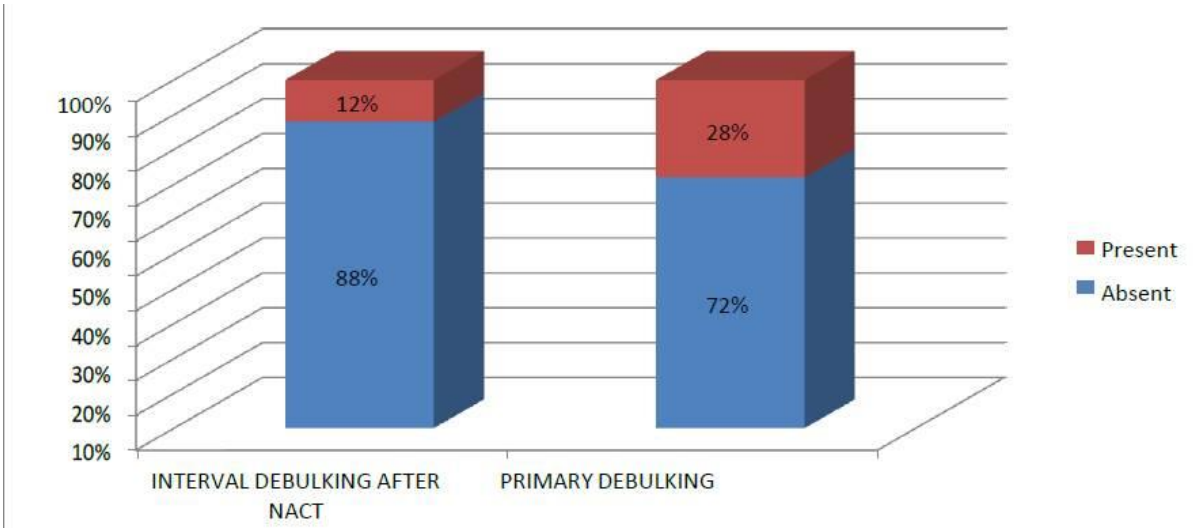

**Graph – 4:** Acitis.



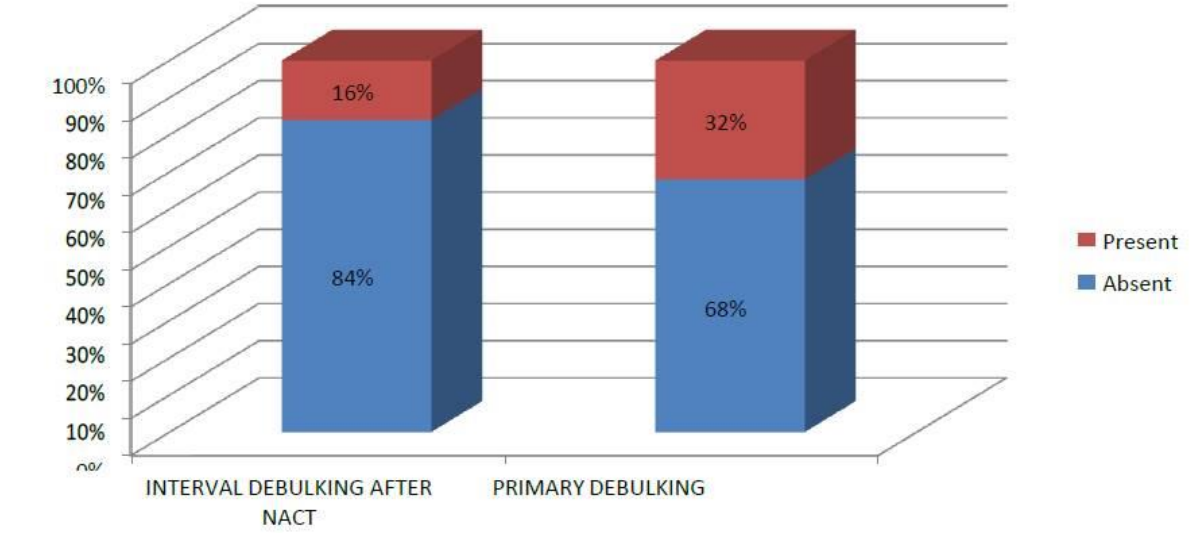

**Graph – 5:** Adhesions.



**Graph - 6:** Injury to adjacent structures.




**Graph – 7:** Post-operative complications.




**Graph - 2** shows most of the women were postmenopausal (44 cases - 88%) in our study. 81% were postmenopausal 15 at the time of diagnosis.

**Graph - 3** shows 75 % of epithelial cancers were serous papillary carcinomas, 16 but in our study serous papillary carcinomas were the most common type carcinomas in 45 cases (90%).

**Graph - 4** shows patients with extensive metastasis or massive ascites before cytoreduction had a poor prognosis even if the patient was cytoreduced to an optimal status. In our study ascitic fluid was present in 20 cases in PD group (80%), and it was present only in 4 cases (25%) of the NACT / IDS group at the time of surgery. Pearson Chi-Square=20.513** p<0.001.

**Graph - 5** shows Adhesions was present in 19 cases (76%) in PDS group but it was seen only in 5 cases (20%) in NACT /IDS group at the time of surgery in our study. Pearson Chi-Square=15.705** p<0.001.

**Graph - 6** shows in our study, injury to adjacent structures was present in 7 cases of PDS group (28%) whereas 3 cases in NACT had an injury. Out of the total 10 cases 2 had bladder injury, 2

had an injury to the small bowel, 3 had a ureteric injury, 2 had a sigmoid colon and the other had a rectal injury.

**Graph - 7** shows Post-op complications were present in 8 cases of PDS group (32%), 4 cases (16%) of NACT/IDS group in our study. Pearson Chi-Square=1.754 p=0.18511.

## Discussion

Epithelial malignancies of the ovarian, fallopian tube and peritoneal origin demonstrate similar clinical characteristics and behavior. So these malignancies have been categorized together as epithelial ovarian cancer (EOC) in clinical trials or clinical practice [9]. According to the World Health Organization report, the annual incidence of EOC is estimated as 225,500 with 140,200 deaths worldwide, affecting 3.7% of all female cancers and 4.2% of cancer deaths. Approximately 80% of EOC cases are diagnosed at an advanced stage, the International Federation of Gynaecology and Obstetrics (FIGO) stage III and IV, resulting in poor survival outcome [10]. Most patients experience disease relapse within the first 5 years despite primary aggressive treatment, whereas only 20–25% of cases are cured. Furthermore, the 5-year survival rate of patients with advanced EOC has not been improved in the last decade. Current standard therapy for patients with advanced EOC is primary debulking surgery (PDS), followed by adjuvant chemotherapy (ACT) with a combination of paclitaxel and carboplatin [11]. Complete or optimal cytoreductive surgery, defined as grossly no residual cancer or <10 mm of residual disease at the end of the surgery, respectively, is known as the most important prognostic factor. Recently, interval debulking surgery (IDS) after a short course of neoadjuvant chemotherapy (NACT) has become an alternative treatment strategy for EOC patients expecting non-optimal cytoreduction during PDS [12]. Tien Le, et al. in their study reported that NACT can decrease tumor volume and increase resectability. Patients may have less intraoperative blood loss, shorter operative time, less ICU admission and shorter hospital stay. in his study reported the resection rate in the group receiving NACT was significantly higher (p=0.04) than that of the conventional group [13]. In our study, optimal cytoreductive debulking that is, no gross residual disease to less than 2 cm residual disease was achieved in 7 cases (28%) out of 25 cases in PDS group, 20 cases (80%) out of 25 cases in NACT/IDS group. Suboptimal cytoreduction that is, gross residual disease to residual disease more than 2 cm was present in 13 cases (52%) of PDS group and 3 cases (12%) of NACT/IDS group. Laparotomy and closure due to frozen pelvis done in 5 cases (20%) of the PDS group and 2 cases (8%) of NACT/IDS group [14]. Vergote I, et al. in his study reported that 35 cases (21%) out of 165 achieved optimal cytoreduction in PDS group, 34 cases (46%) out of 74 cases had optimal cytoreduction in NACT/IDS group 2. Deo, et al. in his study reported that 59 cases (72%) out of 82 cases achieved optimal cytoreduction, 15 cases (18.2%) out of 82 cases achieved suboptimal cytoreduction and 8 cases (9.8) out of 82 cases exploratory laparotomy and closure was performed [15].

## Conclusion

Neoadjuvant chemotherapy is significantly more effective in achieving optimal cytoreduction and reducing the ascitic fluid volume in advanced ovarian cancer. Blood transfusion requirement is significantly less in the neoadjuvant chemotherapy group. Adhesions are found to be significantly less in the NACT group.

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