EVALUATING THE RESULT OF CYTOREDUCTIVE SURGERY AFTER NEOADJUVANT CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER

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A retrospective study of 61 patients was conducted to evaluate the preliminary results of maximal cytoreductive surgery following neoadjuvant chemotherapy for FIGO stage IIIC-IV ovarian cancer from 2019 to 2023. The patients were diagnosed with FIGO staged IIIC (54.1%) and IV (45.9%), confirmed by preoperative histopathology. Elevated CA 125 level (> 1000 UI/ml) was found in 45 patients (73.8%). The rate of patients achieving optimal surgery was 80.4%. The mean surgery time was 134.1 ± 39.1 minutes, the average blood loss in 1 surgery was 171.2 ± 144.9mL. The drainage volume during the first 3 days was 115.4 ± 38.1mL. The patient started passing gas 3.9 ± 1.0 days after surgery, and started walking after 8.3 ± 2.0 days. The discharged day was 10.1 ± 2.1 days. After surgery, only 1 patient had intestinal obstruction, 2 patients had infection, 2 patients had bleeding, 1 patient had bladder dysfunction, and the remaining patients were stable postoperatively.

Keywords: Ovarian cancer, maximal cytoreductive surgery, neoadjuvant chemotherapy.

I. INTRODUCTION

Ovarian cancer is one of the most common malignant gynecological conditions. According to GLOBOCAN 2020, it is the third most prevalent gynecological cancer in Vietnam, with an incidence rate of 2.1 per 100,000 women.[1] Histopathologically, 80 - 90% of ovarian cancers are of epithelial origin, 5 - 10% are germ cell tumors, and approximately 5% arise from stromal tissue. The prognosis for ovarian cancer remains poor, primarily because most cases are diagnosed at an advanced stage, with metastasis already present. Over 70% of patients are diagnosed at stage III or IV, largely due to the deep pelvic location of the ovaries and the nonspecific nature of the symptoms, which are often mistaken for other medical conditions.[2]

Primary maximal cytoreductive surgery followed by adjuvant chemotherapy has traditionally been the standard treatment for advanced-stage ovarian carcinoma.[3,4] However, the success of this approach is often hindered by the extensive tumor burden and the patient's compromised condition, making optimal outcomes challenging to achieve. In recent years, neoadjuvant chemotherapy has emerged as an alternative for patients with advanced ovarian carcinoma who are unlikely to benefit from immediate maximal cytoreductive surgery. Despite this shift, there remains significant debate regarding whether optimal cytoreduction can be consistently achieved and whether the surgical outcomes meet the expected standards.[5-7] Therefore, this study

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aims to assess the early outcomes of maximal cytoreductive surgery following neoadjuvant chemotherapy in patients with FIGO stage IIIC-IV ovarian carcinoma.

II. MATERIALS AND METHODS

1. Subjects

Sixty-one stage IIIC-IV ovarian cancer patients who underwent cytoreductive surgery followed by neoadjuvant chemotherapy at Hanoi Medical University Hospital and K Hospital from January 2019 to June 2023.

Inclusion criteria

Patients with a confirmed diagnosis of FIGO stage IIIC-IV epithelial ovarian carcinoma; Treatment-naive patients; Patients who received neoadjuvant chemotherapy with the paclitaxel-carboplatin regimen (paclitaxel 175 mg/m^2 on day 1, carboplatin AUC5 on day 1, every three weeks for a total of three cycles or paclitaxel 60 mg/m^2, carboplatin AUC2 every week if ECOG performance status 2); Patients who underwent maximal cytoreductive surgery following neoadjuvant chemotherapy; General condition: ECOG performance status 0 - 2, with normal bone marrow, liver, and renal function.

Exclusion criteria

Patients who discontinued treatment for reasons unrelated to disease progression; Incomplete patient records. The patient was not able to undergo optimal debulking surgery due to the surgeon's experience or the underlying medical conditions that did not meet the criteria for surgery

2. Methods

Study Design: A descriptive study.

Sample Size: Convenience sample.

Data Collection

- Clinical and paraclinical characteristics, including age, disease stage at initial diagnosis (FIGO staging was used in this study), and histopathological subtype.

- Postoperative outcomes: residual tumor, postoperative complications (hemorrage, bowel obstruction, infection, bladder dysfunction), surgery outcome (timing of surgery, blood loss, days of recovery).

The treatment process: 5 steps

Step 1: Selection of patients with stage IIIC and IV ovarian carcinoma according to the FIGO classification based on clinical and paraclinical criteria.

Step 2: Administration of neoadjuvant chemotherapy with the Paclitaxel-Carboplatin regimen (Paclitaxel 175 mg/m^2 and Carboplatin AUC5, intravenously administered) every 3 weeks for a total of 3 cycles, or paclitaxel 60 mg/m^2, carboplatin AUC2 every week for 9 weeks.

Step 3: Maximal cytoreductive surgery (debulking surgery) was performed after completing neoadjuvant chemotherapy. Data on blood loss, duration of surgery, and postoperative condition were collected.

Step 4: Postoperative assessment was conducted to evaluate patient condition, recording postoperative complications and recovery indicators.

Step 5: Post-surgery follow-up was conducted to assess patient recovery and determine further chemotherapy.

Data Analysis: Data were processed using SPSS version 22.0.

3. Research ethics

This study was approved by the institutional review board (IRB) at Hanoi Medical University, IRB number was IRB – VN 01001. In addition, the research was approved and supported by the Managing Council of National Cancer Hospital and Hanoi Medical University Hospital.

III. RESULTS

1. Clinical and Paraclinical Characteristics

Table 1. Clinical and Paraclinical Characteristics

	n (%)
Age	
< 50	13 (21.3%)
50 - 59	16 (26.2%)
> 59	32 (52.5%)
Menstrual Status	
Premenopausal	11 (18.0%)
Postmenopausal	50 (82.0%)
Ascites	
Present	41 (67.2%)
Absent	20 (32.8%)
Stage	
FIGO IIIC	33 (54.1%)
FIGO IV	28 (45.9%)
ECOG	
0 - 1	53 (86.9%)
2	8 (13.1%)
CA 125	
> 1000 U/mL	45 (73.8%)
< 1000 U/mL	16 (26.2%)

The average age of the patients was 59.0 ± 10.4 years, with a range from 34 to 84 years old. Of the 61 patients, 50 were postmenopausal. The study cohort included 33 patients with FIGO stage IIIC and 28 patients with FIGO stage IV ovarian cancer. Clinical ascites was observed in 21 patients, and 8 patients had an ECOG performance status of 2. Additionally, 73.8% of the patients had preoperative CA 125 levels exceeding 1000 U/mL.

Table 2. Histopathological results

Histopathology	Number	Percentage (%)
Serous carcinoma	53	86.8
Clear cell carcinoma	4	6.6
Mucinous carcinoma	2	3.3
Endometrioid carcinoma	2	3.3

Histopathological analysis of the study cohort showed that 53 patients (86.8%) had serous carcinoma, while 4 patients (6.6%) had clear cell carcinoma. Mucinous carcinoma and endometrioid carcinoma were each present in 2 patients, representing 3.3% of the cohort for each subtype.

2. Surgical outcome

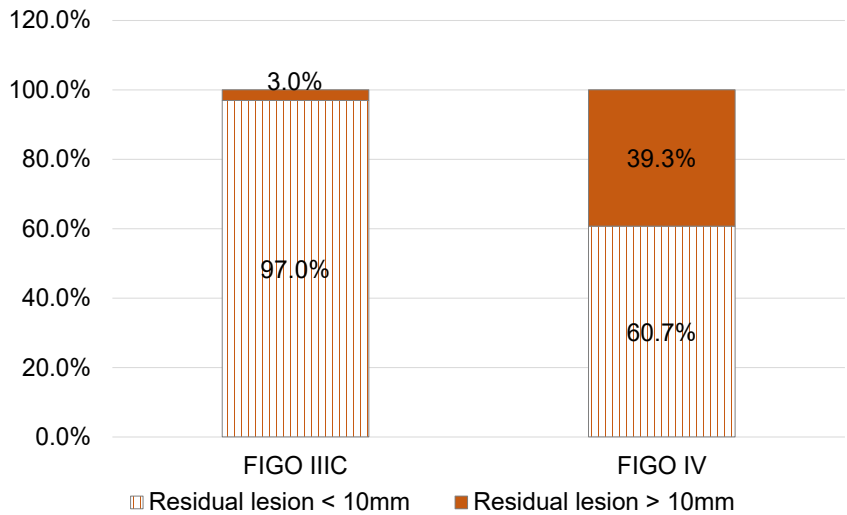

Chart 1. Surgical outcomes of maximal cytoreduction by stage

Among the 61 patients who underwent surgery, 49 patients had residual tumors measuring less than 1cm, corresponding to 58 patients (80.3%) achieving optimal cytoreductive surgery. Conversely, 12 patients (19.7%) had residual tumors greater than 1cm postoperatively. In the FIGO IIIC cohort, the rate of optimal surgery, defined as residual lesions less than 10mm, was 97%. Even among the 12 FIGO IV patients, the majority (60.7%) still achieved optimal cytoreduction.

Table 3. Surgical outcome

	Mean ± SD (Min - Max)
Surgery duration (min)	134.1 ± 39.1 (60 - 250)
Blood loss (ml)	171.2 ± 144.9 (50 - 700)
Average drainage volume (ml)	115.4 ± 38.1 (30 - 200)
Days until drain removal (days)	8.1 ± 2.1 (4 - 14)
Days until first flatus (days)	3.9 ± 1.0 (2 - 7)
Days until ambulation (days)	8.3 ± 2.0 (6 - 13)
Length of hospital stay (days)	10.1 ± 2.1 (6 - 14)

The average surgery duration was 134.1 ± 39.1 minutes, with an average blood loss of 171.2 ± 144.9mL per surgery. The average drainage volume in the first three days postoperatively was 115.4 ± 38.1mL. Patients began passing flatus on postoperative day 3.9 ± 1.0, ambulated by day 8.3 ± 2.0, and had an average hospital stay of 10.1 ± 2.1 days.

Table 4. Surgical complications

Complication	n (%)
Partial bowel obstruction	1 (1.6%)
Hemorrhage	2 (3.3%)
Thromboembolism	0 (0%)
Infection	2 (3.3%)
Stump leakage	0 (0%)
Bladder dysfunction	1 (1.6%)

Postoperative complications are presented in Table 5. One patient (1.6%) experienced partial bowel obstruction, two patients (3.3%) had infections, two patients (3.3%) had hemorrhage, and one patient (1.6%) had bladder dysfunction. No patients required emergency surgery following the initial procedure due to postoperative complications.

IV. DISCUSSION

In our study, the average patient age was 59.0 ± 10.4 years, ranging from 34 to 84 years old. This finding is consistent with the results of Yan Gao (2019), which reported an average age of 58 years, and Vergote (2010), which reported an average age of 63 years in patients undergoing neoadjuvant chemotherapy.[8,9] The average age in our study was higher than other domestic studies, such as of Pham Thi Dieu Ha (2012), which reported an average age of 51.1 years.[10] This difference may be partly explained that neoadjuvant chemotherapy is often prioritized for older patients with poor overall health or comorbidities, making them unsuitable for immediate surgery. Among the 61 patients in our study, 28 had distant metastases (stage IV). The metastatic sites observed included the lungs and pleura (10 patients), liver (13 patients), cervical lymph nodes (4 patients), and spleen (1 patient). The proportion of stage IV patients in our cohort was higher than in the study by Vergote (2010), which reported a rate of 24.3%, but similar to Yong Jae Lee's (2018) study, which reported a rate of 42.5%.[11] Both domestic and international studies have identified the pleura and liver as the most common metastatic sites.[12] Although nearly 50% of our patients were stage IV, most had good overall health, with only 8 patients having an ECOG performance status of 2. While poor general health or comorbidities can limit the suitability for immediate maximal cytoreductive surgery, they also present a challenge for surgery after neoadjuvant chemotherapy.

CA125 (Carcinoma antigen 125) is a protein tumor marker, especially for ovarian cancer. It is typically more concentrated in ovarian cancer cells than in other cell types. CA125 levels are usually measured in blood samples, with normal values typically being below 35 U/mL, depending on the laboratory. Despite the availability of various tumor markers, CA125 remains the most widely used biomarker in ovarian cancer. In advanced stages, the sensitivity and specificity of CA125 for detecting ovarian cancer are approximately 80%. Elevated CA125 levels can also be observed in various benign conditions, such as endometriosis and pelvic inflammatory disease. Serous epithelial ovarian cancers tend to show

elevated CA125 levels (> 85%), while mucinous types exhibit lower elevations. In our study, all patients had CA125 levels exceeding 35 U/mL, with an average level of 2101.6 U/mL at initial diagnosis and 211.4 U/mL before surgery. Most patients exhibited a decrease in CA125 levels following neoadjuvant chemotherapy. According to Pham Thi Dieu Ha, CA125 levels increase with disease progression, with higher levels observed in more advanced stages.[10] Our findings in stage III-IV epithelial ovarian cancer patients are consistent with this conclusion, with 73.8% of patients having CA125 levels above 1000 U/mL. This result aligns with findings from the JCOG0602 study and studies by Vergote (2010), Yong Jae Lee (2018), and Yan Gao (2019).[8,9,11,13]

Histologically, among the 61 patients, 53 (86.8%) had serous carcinoma, 4 (6.6%) had clear cell carcinoma, and both mucinous and endometrioid carcinomas were observed in 2 patients each, representing 3.3% of the cohort for each subtype. Other studies have also shown that serous carcinoma is the most common histological subtype in ovarian cancer, with rates ranging from 58% to 87%. In major global studies on neoadjuvant chemotherapy for ovarian cancer, including EORTC55971, CHORUS, JCOG0602, and SCORPION, high-grade serous carcinoma is also the predominant subtype, with rates ranging from 58.1% to 98.9%.[14]

Neoadjuvant chemotherapy for advanced-stage ovarian cancer, also known as preoperative or induction chemotherapy, has gained increasing attention and is becoming more common in clinical practice in Vietnam. Neoadjuvant chemotherapy is currently indicated for stage IIIC and IV ovarian cancer patients who are unlikely to achieve optimal cytoreduction (defined as no residual tumor or residual lesions < 10mm) based on evaluation by an experienced gynecologic oncologist. It is also indicated for patients with poor overall health or significant comorbidities, making them unsuitable for extensive initial surgery. Our study focused on patients with advanced-stage IIIC-IV disease who were predicted to have a poor prognosis for achieving optimal cytoreduction at the initial surgery. Given the strong evidence supporting the efficacy of the TC (paclitaxel-carboplatin) regimen in adjuvant therapy and the established role of platinum-based agents, paclitaxel-carboplatin remains the most widely used regimen for neoadjuvant chemotherapy. In this study, all 61 patients received this regimen. After completing neoadjuvant chemotherapy, patients were re-evaluated and underwent maximal cytoreductive surgery. As mentioned above, optimal cytoreduction is defined as no residual tumor or residual lesions < 10mm. Achieving optimal cytoreduction is a critical treatment goal for ovarian cancer, as numerous studies have demonstrated its association with improved overall survival (OS) and progression-free survival (PFS). The combination of neoadjuvant chemotherapy and surgery aims to increase the rate of optimal cytoreduction while reducing intraoperative and postoperative mortality and complications.

In our study, 49 out of 61 patients (80.3%) achieved optimal cytoreduction, including 7 patients with complete response (no residual disease and no cancer cell in postoperative specimens) and 42 patients with partial response (residual lesions < 1cm). Twelve patients did not achieve optimal cytoreduction, most of whom were in the FIGO IV group. These patients had unresectable metastatic lesions in the lungs, pleura, liver hilum, and pancreatic head, or multiple small lesions in various segments of the intestine, with residual lesions > 1cm. The rate

of optimal cytoreduction in our study is relatively high at 80.3%, consistent with the SCORPION and JCOG0602 studies, which reported rates of 90.4% and 84%, respectively.[3,14] This result is also consistent with Heriberto's trial, which suggests that neoadjuvant chemotherapy may be a suitable option for patients who are not candidates for immediate surgery.[5] The average surgery duration was 134.1 ± 39.1 minutes, with an average blood loss of 171.2 ± 144.9mL per surgery. Patients recovered relatively quickly, with the first flatus observed 2 - 3 days after surgery, and ambulation resumed within the first week. The average hospital stay after surgery was also relatively short, at 10.1 ± 2.1 days. Postoperative complications were minimal, with only one patient experiencing partial bowel obstruction, two patients developing infections, two patients experiencing bleeding, and one patient developing bladder dysfunction. There were no death, and all complications were managed medically without the need for additional surgical intervention. Our findings align with those of Vergote (2010), who conducted a study on 670 patients with FIGO IIIC-IV ovarian cancer.[9] That study reported a postoperative mortality rate (defined as death within 28 days of surgery) of 2.5% in the primary surgery group and 0.7% in the group undergoing surgery after neoadjuvant chemotherapy. Postoperative bleeding (grade 3 - 4) occurred in 7.4% and 4.1% of patients in the primary surgery and neoadjuvant chemotherapy groups, respectively; postoperative infection rates were 8.1% and 1.7%, and vascular complications occurred in 2.6% and 0% of patients, respectively. These initial results suggest that neoadjuvant chemotherapy followed by surgery can reduce postoperative mortality and complications.

V. CONCLUSION

This study demonstrates that maximal cytoreductive surgery following neoadjuvant chemotherapy for patients with FIGO stage IIIC-IV epithelial ovarian cancer achieves an optimal cytoreduction rate of 80.3%. Among the 61 patients, 49 achieved optimal cytoreduction with residual tumors measuring less than 1cm, including 7 patients with no residual disease. Although some patients had larger residual tumors, most belonged to the FIGO stage IV group with unresectable metastatic lesions.

The average surgical duration was 134.1 minutes, with an average blood loss of 171.2mL, indicating a safe and efficient surgical process. Postoperative complications were minimal, and no death occurred during the study. These findings suggest that neoadjuvant chemotherapy is a viable treatment option for patients with advanced ovarian cancer, and further multicenter studies are recommended to evaluate long-term outcomes and optimize patient selection criteria for neoadjuvant chemotherapy.

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