

# EVALUATION OF THE RESULTS OF LAPAROSCOPIC DEBULKING SURGERY IN THE MANAGEMENT OF ADVANCED OVARIAN CANCER AFTER NEOADJUVANT CHEMOTHERAPY AT HUE CENTRAL HOSPITAL

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## ABSTRACT

**Objective:** The purpose of this study was to evaluate the feasibility and the effect of the laparoscopic debulking surgery in the treatment of advanced ovarian cancer after neoadjuvant chemotherapy. **Methods:** We performed a retrospective review of laparoscopic approach in patients with histologically confirmed epithelial ovarian cancer (International Federation of Gynaecology and Obstetrics stages IIIC-IV) who received 3 courses of neoadjuvant chemo-therapy, from January 2012 to January 2018, at the Department of Obstetrics and Gynaecology, Hue Central Hospital.

**Results:** A total of 32 patients were included. The median age was 51 years (range, 25-67 years), median body mass index was 24.4 kg/m<sup>2</sup> (range, 20-41 kg/m<sup>2</sup>). All patients had good clinical response to 3 cycles of neoadjuvant chemotherapy. Most women underwent a complete debulking surgery with no residual disease (56.25%). The median operating time was 150 minutes (range, 75-330 minutes), the median blood loss was 85 mL (range, 55-220 mL). The median number of removed pelvic lymph nodes was 14 (range, 09-21). There was 1 (3.13%) intraoperative complication and 2 (6.26%) postoperative short-term complications. The median length of hospital stay was 5 days (range, 4-13 days). The median follow-up was 18 months (range, 5-56 months). Twenty-eight patients are free from recurrence at this time.

**Conclusions:** Laparoscopic cytoreduction when performed by skilled surgeons, seems feasible and may decrease the impact of aggressive surgery in patients with advanced ovarian cancer after neoadjuvant chemotherapy, is an attractive alternative to the traditional abdominal surgical approach. The significant advantages of this approach are less invasive surgery, less blood loss during surgery, short recovery time.

**Key words:** Ovarian cancer, Laparoscopic cytoreduction, Neoadjuvant chemotherapy

## I. INTRODUCTION

Although the conventional treatment of advanced ovarian cancer is based on associating surgery and chemotherapy, the residual of disease after surgery seems to be the most important factor affecting survival time of the patient. Over the last few decades, the use of surgery after a few cycles of neoadjuvant chemotherapy in patients with advanced stages (International Federation of Gynaecology and Obstetrics [FIGO] stage IIIC/IV) has been proposed to increase the rate of the optimal debulking and reduce the number of complications [1-4]. Recent laparoscopic surgery performed

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in ovarian cancer shows similar results to open abdominal surgery and patients have the better profit from the superior advantages of a minimally invasive surgery [5,6].

At Hue Central Hospital, we have performed endoscopic surgery for the treatment of ovarian cancer since January 2012 with the help of laparoscopic experts from the Kingdom of Belgium, until now has been over 6 years. This research project aims to:

1. Investigate the safety, the feasibility and the effect of the laparoscopic debulking surgery in the treatment of advanced ovarian cancer (IIIC-IV stages) after neoadjuvant chemotherapy.

2. Analysis of general characteristics, outcomes of postoperative survival time in total number of patients studied.

## **II. MATERIALS AND METHODS**

### **2.1. Subjects**

All patients in the advanced stage (FIGO IIIC-IV) had a histopathological diagnosis of ovarian carcinoma from January 2012 to January 2018. Patients were treated 3 cycles of neoadjuvant chemotherapy and then reassessed with serum CA-125 and CT scan before and after chemotherapy. The criterias for neoadjuvant chemotherapy: in the case of evaluating that the laparoscopic debulking surgery is difficult and is not optimal [7],[8].

Criteria for laparoscopic surgery patients: absolute white blood cell count above 2000/mL, platelet count above 100.000/mL, and normal kidney, liver and heart function, patients with a clinically optimal response to neoadjuvant chemotherapy.

Exclusive criteria: severe cardiopulmonary disease such as myocardial infarction, recurrent angina, severe obstructive pulmonary disease, systemic infection.

### **2.2. Methods:**

Retrospective, descriptive, cross-sectional study was carried out in 32 patients. The parameters

evaluated in the study included age, body mass index (BMI), FIGO clinical stage, tumor, response to chemotherapy assessed in combination with serum CA-125 levels and CT scans, before and after treatment. Parameters in surgery include surgery time, blood loss and complications. Blood transfusion is indicated if the hemoglobin value is less than 7g/l, hospital stay, average follow-up time, relapse, DFI, and OS.

### **Neoadjuvant chemotherapy and evaluation of clinical response:**

Carboplatine (AUC 6) was combined with paclitaxel (175 mg/m<sup>2</sup>) for 3 cycles of 21 days. Antiangiogenic treatment with bevacizumab (15 mg/kg) was initiated during the first 3 cycles. Clinical response assessment was based on serum CA-125 levels and chest and abdominal computed tomography for 30 days.

### **Laparoscopic debulking surgery after Neoadjuvant chemotherapy:**

Laparoscopic debulking surgery is performed within 4 weeks since the last chemotherapy cycle, and in the post operative time, the patient would be treated with 3 cycles of adjuvant chemotherapy:

#### **Surgical procedure:**

##### **- Introducing through the abdomen wall**

With one 10-mm Trocar at the navel site and three 5-mm trocars at the lower abdomen area. During endoscopy, we look carefully to check the entire peritoneal cavity. When finished, checking again to make sure the blood was carefully controlled. Here we do not put any drainage as well as any treatment of postoperative thromboprophylaxis

##### **- Peritoneal lymphadenectomy**

The dissection begins by opening the broad ligament and lateral pelvic peritoneum between the round ligament and the infundibulopelvic ligament. Lymph nodes and adipose tissue are surgically removed from the posterior obturator fossa, when exposed to vascular and nerve of the pelvis and the obturator fossa. We performed this procedure up

to the bifurcation of common iliac artery and the lower orifice of the inguinal canal. The cavities next to bladder and rectum were also examined and carefully dissected. The ureter was observed along the peritoneal line at the level of the bifurcation of common iliac artery.

**- Laparoscopic total hysterectomy:** Firstly putting an uterine manipulator, then surgical procedures in turn include: severing the round ligament, dissecting the upper broad ligament, severing the infundibulopelvic ligament and the bilateral appendages, cutting the sacro-utero-ligament, the removal of the bladder from the lower uterus and upper vagina, sealing and cutting the vagino- utero- vasculars, opening of the vagina, Taking the uterus and the omentum after omentectomy out through the vagina, closing the vaginal vault, laparoscopically examining the vaginal vault and ureter, closing the trocar orifices.

### **- Radical omentectomy**

**Surgical time** is calculated from the time of incision to the last closing skin suture. The length of hospitalization is from the first postoperative day to discharge. Complications during and after surgery if there is organ damage and assessed according to the Clavien-Dindo classification [9]. The patients had more 3 cycles of adjuvant chemotherapy in post operation.

**Postoperative Follow-up:** All patients are evaluated regularly at the end of treatment. Clinical examination, CA-125 and ultrasound are performed every 3 months and computerized tomography is performed every 6 months for the first 2 years of follow-up.

## **III. RESULTS**

### **Patient characteristics**

From January 2012 to January 2018, 32 patients were included in the study. 27 patients with ovarian carcinoma at IIIC or IV stage who underwent initial laparoscopic surgery for diagnosis at Hue Central

Hospital. Five patients (15.6%) of the 32 patients underwent primary surgery in lower level hospitals and were subsequently transferred to our hospital: 3 cases of bilateral oophorosalingectomy with open abdominal laparostomy, and 1 case of total hysterectomy with bilateral oophorosalingectomy and 1 case of laparoscopic ovarian cystectomy. The median age was 51 years (range 25-67 years) and the average BMI was 24.4 kg/m<sup>2</sup> (ranging from 20-41kg/m<sup>2</sup>). Fifteen patients (46.8%) had open abdominal surgery. All patients were evaluated for toxicity and response to chemotherapy (Table 1).

*Table 1: Patient characteristics*

Characteristics	
Patients	32
Median age (range)	51 (25-67)
Prior abdominal surgery, no. (%)	15, (46.8)
average BMI (range)	24.4 (20-41)
Histology, No. (%)	
Endometrioid	1 (3.1)
Serous	25 (78.1)
Clear cell	6 (18.8)
Grading, No. (%)	
G2	8 (25.0)
G3	24(75.0)

### **Clinical evaluation after Neoadjuvant chemotherapy**

All 32 patients have a good response to 3 cycles of neoadjuvant chemotherapy which showed good tolerance.

### **Operative Parameters**

All patients were operated with complete cytoreduction, residual tissue is trivial. Type of surgery is detailed in the Table 2.

*Table 2. Type of surgery*

Characteristics	%
Unilateral salpingo-oophorectomy	6 (18.75)
Biteral salpingo-oophorectomy	4 (12,5)
Hysterectomy	32 (100)
Omentectomy	32 (100)
Pelvic lymphadenectomy	16 (50)
Trachelectomy	1 (3.13)

Average surgery time is 150 minutes (range 75-330 minutes), average blood loss is 85 ml (range from 55-220 ml); No patient needed blood transfusions during surgery, only one patient received transfusions after surgery. The average number of lymph nodes removed was 14 (range 9-21). One case (3.13%) had damage at the left hypogastric vein that had to change to open surgery

for hemostasis . Another case must be switched to open surgery due to severe adhesion. There were 2 cases (6.26%) having hematoma at the vaginal vault after the surgery and were successfully managed by ultrasonic drainage aspiration. One case that occurred ascite due to lymphatic vascular oedeme was treated with medical treatment (Table 3). The mean hospital stay was 5 days (range 4-13 days).

*Table 3. Surgical results*

<b>Characteristics</b>	
Operative time, median (range), min	150 (75-330)
Blood loss, median (range), mL	85 (55-220)
Pelvic lymph nodes, median (range)	14 (9-21)
Major intraoperative complications, n (%)	1 (3,13)
Major early postoperative complications, n (%)	2 (6,26)
Major late postoperative complication, n (%)	0
Blood transfusion, n (%)	1 (3,13)
Conversion to laparotomy, n (%)	2 (6,26)
Hospital stay, median (range), day	5 (4-13)

#### **Further Management and Follow-Up**

Eighteen patients (56.25%) did not show any residue on histopathological examination and fourteen patients showed histologically residual tumors (43.75%). All the patients received more 3 cycles of adjuvant chemotherapy in post operation. However, two cases had to be discontinued due to hematologic toxicity at level 3 after the fourth and fifth cycles. The mean follow-up was 18 months (range 5-56 months). 28 patients had no relapse at the time of this report. One patient had a pelvic lymph node recurrence with a disease-free survival time (DFI) of 8 months and was still alive and continuing chemotherapy. Three patients died of peritoneal recurrence with DFI at 6, 12, and 14 months, respectively, and with OS at 23, 31, and 54 months respectively.

#### **IV. DISCUSSION**

This study demonstrates the feasibility of laparoscopic debulking surgery in advanced

ovarian cancer after neoadjuvant chemotherapy, reduced blood loss and complications during and after surgery. The issue of whether or not optimal surgery of cancerous tumors during surgery at the first time or after neoadjuvant chemotherapy remains the most important prognostic factor in the treatment of advanced ovarian cancer. The widespread of minimally invasive surgery in the past few decades has seen new advances in the treatment of gynecologic cancers, thanks to its superiority in reducing complications and time of recovery from surgery. Although laparoscopic surgery is a widely accepted as method of treating endometrial cancer and cervical cancer, it has not been widely used in the treatment of ovarian cancer at advanced stage [10,11]. The application of laparoscopic surgery in the treatment of early ovarian cancer shows that this is a safe, feasible and comprehensive treatment. Recent advances in instruments and endoscopic imaging techniques have allowed the application of laparoscopic

surgery even in the advanced stages of ovarian cancer. Amara et al. [12] described the first report of five patients with advanced ovarian cancer who underwent successful laparoscopy. In our study, the majority of patients had an optimal cytoreductive surgery and an average non recurrence period was rather high, similar to the results reported in other studies [13,14]. This can be explained as having the combination of optimal surgery and good response to chemotherapy in our patients. The results of the study also showed that good cytoreduction in surgery, leaving no residual tumor after surgery, will significantly improve survival rate. Other relevant factors to achieve the highest cytoreduction include time, appropriate surgery and chemotherapy. On the other hand, the choice of a laparoscopic surgical method may improve the morbidity of these high-risk patients. Our outcomes in the study, including blood loss during surgery, hospital stay, and complications during and after surgery, were similar and consistent with the results of several other studies over the world [15].

## V. CONCLUSION

Laparoscopic surgery in patients with advanced ovarian cancer after neoadjuvant chemotherapy is performed by well-trained surgeons and in a select group of patients, which appears to be feasible and may alleviate some of the negative effects of open abdominal surgery on patients after neoadjuvant chemotherapy. The advances in laparoscopic techniques allow that laparoscopic surgery were performed on selected ovarian cancer patients. Due to the long duration of surgery, important predictive factors such as illness, age, burden of disease, metastatic location, and condition of the surgeon performing surgery should be considered carefully to determine the endoscopic approach in a patient so that optimal cytoreduction can be achieved during this time. Although the survival outcome was satisfactory, however, the number of patients studied was still small, so the method of laparoscopic debulking surgery for advanced ovarian cancer after neoadjuvant chemotherapy should be continued and further evaluated in future studies.

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