

Ovarian cancer: focus Neoadjuvant chemotherapy and primary cytoreduction surgery in advanced ovarian cancers

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Abstract:

Background: Complete cytoreductive surgery is the cornerstone of treating advanced ovarian cancer with platinum salt chemotherapy. The tumor residue after maximal cytoreduction surgery is an essential prognostic factor for survival. The chronology of treatment is still debated, French and especially American recommendations place primary surgery as the standard and interval surgery as an option when initial surgery is not possible from the outset. The goal of resectability must be the same regardless of the option chosen, namely obtaining an infra-centimetric or ideally zero residue with a lower morbidity rate. Care must of course be discussed in a multidisciplinary consultation meeting.

Keywords: ovarian cancer, cytoreduction surgery, neoadjuvant chemotherapy, tumor residue.

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I. Introduction

Epithelial ovarian cancer (ECC) affects one in 70 women in industrialized countries. It is the 5th most common cancer in women and represents the 4th cause of death from female cancer. In France in 2017, its incidence was around 4714 new cases and 3111 deaths. In Algeria, it is in 6th place with 3200 deaths per year. It mainly concerns women after menopause. (1)

The prognosis of patients with ovarian cancer depends on the stage of the FIGO (International Federation of Obstetric Gynecology), the histological grade, the histological subtype, the age of the patient and the residual tumor mass after surgery (6). It remains grim with an overall 5-year survival of 30% all stages and the majority of deaths occur within the first two years after diagnosis. Three quarters of the patients are diagnosed at an advanced stage (stage IIIc and IV of FIGO), that is to say already a spread of the disease over the entire surface of the peritoneum and retro peritoneum. These patients have an overall 5-year survival of less than 20%. (1.3)

The management of patients with advanced ovarian cancer consists of optimal complete surgery (notumor residue) followed by six courses of chemotherapy based on platinum salts. The surgery must begin with a complete exploration of the entire abdominal cavity under laparoscopy by establishing a resectability score (Fagotti score) or by medianlaparotomy, the Sugarbaker score. It would include at least peritoneal cytology, total hysterectomy, bilateral adnexectomy, resection of all tumor sites, infra-colic omentectomy, pelvic and lumbar-aortic lymph node dissection. (6)

The management of these cancers is very heterogeneous both surgically and medically (chemotherapy) or the therapeutic sequence (primary surgery versus interval surgery).

II. Role of primary debulking surgery

The first cytoreductive surgery or debulking followed by adjuvant chemotherapy consists in a maximum ablation of all the tumor tissue and its metastases, this process was described by Tom Griffiths in 1975. He quantified the benefit of a surgery of first cytoreduction in a retrospective series of 102 patients treated at Boston hospital. Griffiths had reported better survival when optimal cytoreduction was done by leaving a tumor residue <1.5 cm in diameter at the end of the operation. (2,16)

Although no prospective randomized study has yet formally proven that primary cytoreduction surgery improves the prognosis in these patients (2). Followed by paclitaxel and platinum-based chemotherapy, this surgery is the standard treatment for advanced epithelial ovarian cancer (CEO).(12)

It is therefore fundamental to ensure the most complete tumor reduction possible with obtaining a remainder of less than one centimeter (optimal surgery), or even ideally zero (absence of macroscopic residue). When there are multiple excisional procedures, surgery can be burdened with a non-negligible complication rate, with postoperative mortality of around 2% and morbidity of around 30% (especially hemorrhagic and infectious). (4)

In addition, when this initial surgery cannot be performed optimally, either because certain tumor areas are not immediately resectable or because the ideal conditions are not met (4), then a tumor reduction surgery called the interval performed after three courses of chemotherapy has been proposed.

III. Role of neoadjuvant chemotherapy followed by cytoreductive surgery or interval surgery

Over the past decades, neoadjuvant chemotherapy (NAC) followed by interval debulking surgery has been increasingly used for patients with bulky disease not suitable for optimal cytoreduction or who may require extensive procedures to achieve optimal resection. The number of cycles of chemotherapy administered before surgery appears to be of clinical relevance, as each increase in cycles of preoperative chemotherapy beyond cycle 3 to cycle 4 has a detrimental effect on overall survival (OS). (8) Therefore, maximum surgical effort should be undertaken as early as possible in these patients.

Compared to primary surgery, recent research has shown that neoadjuvant chemotherapy is associated with a high and optimal rate of cytoreduction, low postoperative morbidity and good quality of life. (5) However; it is confirmed by the registers of controlled and randomized clinical trials that ANC does not improve the overall survival and the survival without recurrence compared to the first surgery. (5)

Currently; the guidelines of the Gynecologic Oncology Society (SGO) and the American Society for Clinical Oncology (ASCO) have recommended neoadjuvant chemotherapy for patients with a high perioperative risk and a low chance of obtaining optimal surgery. (5,13)

Two large randomized trials (EORTC 55971: European Organization For Research and Treatment of Cancer) published in 2010 and (CHORUS) published in 2015 (10,11,17) showed that neoadjuvant chemotherapy followed by interval surgery is not inferior in recurrence-free survival (SRFS) and OS compared to first surgery in patients with advanced ovarian cancer. In addition, recent clinical investigations seem to suggest that recurrence after neoadjuvant chemotherapy and interval surgery is more biologically aggressive than recurrence after primary surgery. (10,11,17,18)

IV. Conclusion

Surgery remains the gold standard for advanced stage ovarian cancer, however neoadjuvant chemotherapy is a therapeutic option that can reduce morbidity and mortality and increase the rate of cytoreduction surgery. We found that patients with FIGO stage IIIc ovarian cancer with less extensive metastatic disease had better survival after primary surgery, while patients with stage IV and extensive metastatic disease had better survival after neoadjuvant chemotherapy.

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