Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Ovarian Cancer: Experience in France

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Summary

Epithelial ovarian cancers (EOC) represent 80%–90% of all ovarian malignancies, and they are the most common cause of death for all gynecological tumors in the Western world (1). The majority of patients have an advanced Federation of Gynecology and Obstetrics (FIGO) stage III or IV disease at presentation, but the disease is often confined to the peritoneal cavity (2). Current standard treatments of these patients consist of initial cytoreductive surgery (CRS) to <1-cm residual nodules, followed by combination systemic chemotherapy with a taxane and platinum analogue, either carboplatin or cisplatin.

Our experience in France with a phase II prospective single-center study shows that the population is inhomogeneous, and >58% of patients underwent CRS and HIPEC after >2 prior recurrences and >2 laparotomies. Because of these multiple recurrences before inclusion, it was not possible to calculate the progression-free interval (PFI). In the literature, most of the series evaluating CRS alone are dedicated to secondary CRS, meaning that the patients are experiencing their first recurrence. The only feasible comparison between secondary CRS alone and this study could be on the completeness of cytoreduction, which appears as the most important prognostic factor. The present phase II study clearly underlines that combined salvage therapy can achieve long-term survival in some patients with second, third, or fourth locoregional recurrence from ovarian cancer.

Key Words: Advanced ovarian cancer; peritoneal carcinomatosis; cytoreductive surgery; hyperthermic intraperitoneal chemotherapy.
1. INTRODUCTION

For advanced EOC, even optimal CRS and optimal systemic chemotherapy may result in cancer recurrences in 30%–50% of cases (3). Although the concept of CRS with a goal of leaving residual tumor masses <1 cm in diameter was first introduced in 1975 (4), maximal initial CRS was found to be the most powerful determinant of survival in a recent meta-analysis (3).

Although primary treatment for advanced EOC is now consensual, two clinical settings remain controversial: (1) patients undergoing a second-look laparotomy with persistent large macroscopic disease on the peritoneum (chemoresistant patients), and (2) patients who develop intraabdominal recurrent disease >6 mo after a complete response to standard primary therapy. Other systemic chemotherapy courses (switching from paclitaxel/platinum to other drugs) or “repeated-CRS” could be proposed in these 2 clinical settings. The impact of “repeated CRS” (second-, third-, fourth-look, etc.) for chemoresistant patients and for those with recurrent disease is still controversial.

Considering the fact that recurrent advanced ovarian cancer is mainly a locoregional disease involving the peritoneum and the adjacent intraabdominal organs, we designed a prospective phase II study to evaluate repeated CRS combined with hyperthermic intraperitoneal chemotherapy (HIPEC). The rationale for combining CRS and HIPEC is based on, first, the reported results of secondary CRS in EOC (5); second, the reported results of CRS combined with HIPEC for PC arising from digestive cancers (6); third, the theoretical advantage of combining hyperthermia and chemotherapy through the IP route; and fourth, the pharmacokinetic advantage of IP cisplatin (7).

2. METHODS AND PATIENTS

Our experience in France with a phase II prospective single-center study is described here. Inclusion criteria were as follows:

1. patients between 18 yr and 75 yr of age,
2. patients with advanced EOC cancer who were found to have large macroscopic residual intraabdominal masses at the second-look surgery,
3. patients with advanced recurrent epithelial cancer after a PFI of at least 6 mo,
4. patients with advanced re-recurrent epithelial cancer after >3 surgical looks and/or >3 systemic chemotherapy lines,
5. patients with no extraabdominal metastases on preinclusion thoracic and cerebral CT scan,
6. patients with a World Health Organization index of <2,
7. patients with satisfactory cardiorespiratory and renal status,
8. and informed consent.