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Peritonectomy procedures and HIPEC in the treatment of peritoneal carcinomatosis from ovarian cancer: Long-term outcomes and perspectives from a high-volume center

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Abstract

Background: Cytoreductive surgery with peritonectomy procedures and hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) represents a radical therapeutic approach to achieve complete cytoreduction in ovarian peritoneal carcinomatosis. The aim of the present study was to analyze the outcomes obtained by the application of these procedures in a single center with extensive experience treating peritoneal carcinomatosis.

Patients and methods: A series of 218 consecutive patients diagnosed with peritoneal carcinomatosis from primary or recurrent ovarian cancer (FIGO stage IIIC–IV) and treated with CRS + HIPEC between January 1996 and June 2012 were included in this observational study.

Results: Peritoneal carcinomatosis was treated primarily in 56% (124/218) of the cases and recurrently in 43% (94/218). A total of 42/218 patients (19%) presented with FIGO stage IV. Compared to recurrent cases, patients with primary ovarian carcinomatosis were older and presented higher Peritoneal Cancer Index (PCI) and percentage of FIGO stage IV; however, no significant differences in survival (5-year overall survival in patients with R0 cytoreduction, 63% and 56%, respectively) were observed. Cytoreduction score, PCI, lymphatic involvement and surgical morbidity ≥Grade III were statistically significant prognostic factors for survival in both univariate and multivariate analysis.

Conclusions: CRS + HIPEC treating macroscopic and microscopic disease is currently an excellent surgical approach to achieve high rates of complete cytoreduction and improve survival in patients with peritoneal carcinomatosis from ovarian cancer. In order to minimize the high potential morbidity of these procedures, CRS + HIPEC should be performed in highly experienced centers.

Keywords: Hyperthermic intraperitoneal chemotherapy; Peritoneal carcinomatosis; Peritonectomy; Ovarian cancer

Introduction

Ovarian cancer is the fifth cause of death from cancer in women, being the most frequent cause of death among gynecological malignancies in developed countries.[1] Unfortunately, the majority of patients will present advanced-stage disease at initial diagnosis, a fact which is intimately related to a poor prognosis. Despite a good response to

Abbreviations: CRS, cytoreductive surgery; CRS + HIPEC, cytoreductive surgery with peritonectomy procedures and hyperthermic intraperitoneal chemotherapy; HIPEC, hyperthermic intraperitoneal chemotherapy; LS, lesion size; OS, overall survival; PCI, Peritoneal Cancer Index.

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primary treatment, most women with advanced-stage disease will experience relapse, and only 20–25% of patients can be expected to survive long-term.[2]

Residual disease after cytoreductive surgery (CRS) for advanced ovarian cancer is defined by the diameter of the largest remaining tumor. Since this is one of the most important prognostic factors, complete cytoreduction must be the objective during surgery.[3–5] Nevertheless, R0 cytoreduction may be challenging in some instances, and standard surgical procedures may fail to remove the entire tumor burden (including non-visible remaining disease). In order to succeed in this scenario, numerous institutions employ CRS with peritonectomy procedures and hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) as described by Sugarbaker two decades ago.[6] This therapeutic approach, which is also applied in the treatment of peritoneal metastases of intestinal origin, is especially interesting in ovarian cancer due to its characteristic locoregional dissemination without initial distant metastases, its frequent chemosensitivity, and its adequate response to postoperative intraperitoneal chemotherapy as shown in several trials.[7] Hence, advanced ovarian cancer could become over the years a paradigm for the utility of CRS + HIPEC.[8]

Although treatment with CRS + HIPEC in patients with ovarian peritoneal carcinomatosis may improve survival rates,[9–13] this scheme is not widespread because most of the studies encouraging its use are retrospective. Nonetheless, Spiliotis et al. have recently published the first randomized study in recurrent epithelial advanced ovarian cancer confirming the benefits of CRS + HIPEC.[14] Currently ongoing clinical trials (CHORINE, CHIPOR, and OVHIPEC) may add more evidence of the importance of these procedures in the treatment of advanced ovarian cancer.

The aim of this study was to analyze the outcomes and the prognostic factors for survival in a large series of patients treated with CRS + HIPEC for peritoneal carcinomatosis from ovarian cancer in a Surgical Oncology Unit with extensive experience in this radical treatment.

Patients and methods

Patients and study design

A retrospective observational study from a prospective database (January 1996–June 2012) was conducted. All cases were discussed in a pretreatment multidisciplinary committee. All subjects met the following inclusion criteria: i) histological confirmation of peritoneal carcinomatosis from epithelial ovarian cancer (including both primary and recurrent ovarian cancer), ii) treatment with CRS + HIPEC, iii) FIGO stage IIIC or FIGO IV with response to neoadjuvant intravenous chemotherapy or complete cytoreduction during radical surgery, iv) Eastern Cooperative Oncology Group (ECOG) performance status grade 2 or less, v) no significant previous organ dysfunction, and vi) completed informed consent form. The exclusion criteria were: i) presence of extra-abdominal metastatic disease without response to neoadjuvant chemotherapy based on CT/PET scan or with incomplete resection, ii) patients with tumor progression despite neoadjuvant chemotherapy, iii) significant organ dysfunction (cardiovascular, respiratory, renal or hepatic), and iv) coexisting malignancy without curative treatment.

All patients included in the recurrent ovarian cancer group presented her first relapse. Follow-up was continued until June 2014.

Neoadjuvant chemotherapy

Following our protocol for advanced ovarian cancer, all patients with primary ovarian cancer FIGO stage IV received from 4 to 8 cycles of carboplatin-plus-paclitaxel-based neoadjuvant chemotherapy.[15] All cases included in the present study showed appropriate response (i.e. radiological tumor stabilization or regression or to FIGO stage III). Patients with primary ovarian cancer FIGO stage IIIC with suspicion of high Peritoneal Cancer Index (PCI) by imaging tests received the same neoadjuvant regimen but fewer cycles (3–4, with a maximum of 6 cycles). Finally, when peritoneal carcinomatosis was a consequence of recurrent ovarian cancer, all patients received preoperative chemotherapy, and the regimen depended on the previous treatment received by each patient.

Surgical procedure (CRS + HIPEC) and postoperative chemotherapy

Tumor burden was estimated by the PCI. This index quantitatively combines the distribution of tumor throughout 13 abdominopelvic regions with a lesion size (LS) score (right upper, epigastrium, left upper, right flank, central midline abdominal, left flank, right lower, pelvis, left lower, upper jejunum, lower jejunum, upper ileum and lower ileum). LS-0 indicates no implants, LS-1 implants less than 0.25 cm, LS-2 between 0.25 and 2.5 cm, and LS-3 greater than 2.5 cm. The LS scores are summated for all abdominopelvic regions. A numerical score from 0 to 39 indicates the extent of the disease in the abdominal cavity.

Patients with primary ovarian cancer underwent total hysterectomy and bilateral salpingo-oophorectomy. In those patients with recurrent ovarian cancer who had undergone previous conservative surgery, hysterectomy and/or bilateral salpingo-oophorectomy were completed. In addition, all subjects underwent *pelvic or infra-abdominal peritonectomy*, including complete exeresis of the peritoneum from pelvic to bilateral iliac fossae by full centripetal dissection, complete greater omentectomy, appendectomy, and anterior resection of the rectum if involved. According to their PCI and tumor involvement (peritoneal resection was limited to the infiltrated regions), some patients