



Secondary cytoreductive surgery for isolated lymph node recurrence of epithelial ovarian cancer: A multicenter study

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Abstract

Introduction: Chemotherapy is the standard treatment of recurrent epithelial ovarian cancer (EOC), but its use in nodal relapses is still debated. On the other hand, the role of secondary cytoreductive surgery (SCS) remains controversial. Aim of this study is to evaluate feasibility and outcomes of SCS for the specific setting of recurrent ovarian cancer, exclusively relapsing in lymph nodes.

Patients and methods: We conducted a retrospective analysis in five Italian Institutions (University of Torino, INT of Milano, CRO of Aviano, University of Pisa and INT of Napoli) from 2000 to 2012. Patients with EOC who underwent secondary surgery for isolated lymph node recurrence (ILNR) were selected.

Results: Seventy-three patients were identified. At first diagnosis, patients received debulking surgery and platinum-based chemotherapy. The median disease free interval from completion of primary chemotherapy to nodal recurrence was 18 months. Nodal recurrence was para-aortic in 37 patients (50.7%), pelvic in 21 (28.8%), pelvic and para-aortic in 9 (12.3%), pelvic and inguinal in 3 (4.1%) and inguinal in 3 (4.1%). During SCS, in 1 patients nephrectomy was necessary for renal vein injury. No significant postoperative morbidity occurred. Median follow-up is 50 months. After secondary surgery, 32 (43.8%) are alive without disease, 18 (24.6%) are alive with disease and 23 patients (31.5%) are dead of disease. Five-year overall survival from the time of treatment of recurrent disease is 64%.

Conclusions: Secondary surgery for ILNR of ovarian cancer is feasible, safe, with low morbidity and it is associated with a favorable outcome.

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Keywords: Epithelial ovarian cancer; Secondary cytoreductive surgery; Isolated lymph node recurrence

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Introduction

Epithelial ovarian cancer (EOC) is the first cause of death from gynecological malignancies. Due to the lack of specific symptoms in early disease, more than two thirds of EOC are diagnosed in advanced stage. After radical primary surgery and platinum based chemotherapy, between 25% and 75% of the patients will eventually relapse.^{1,2}

Nowadays, chemotherapy still is the standard treatment of recurrent ovarian cancer. Cytoreductive surgery, is accepted as the main treatment of primary ovarian cancer, but it is still discussed in recurrent disease. Secondary cytoreductive surgery (SCS) is defined as surgery performed after the completion of the primary treatment and a disease free period. There is no level I evidence to demonstrate a survival advantage associated with secondary cytoreductive surgery in women with recurrent ovarian cancer.³ Until data from ongoing trials will be mature (GOG 213 and AGO-OVAR DESK-TOP 3), the evidence is based almost entirely on retrospective studies, suggesting a benefit of SCS in selected patients with long disease free interval, resectable disease (based on imaging), absence of ascites, a limited number of metastatic sites and a good performance status.^{4,5} SCS aims at the prolongation of survival and at the improvement of quality of life and cancer-related symptoms. Pelvis, peritoneum, pleural effusion, liver, lung, lymph nodes and central nervous system are the most frequent sites of recurrence.⁶ Among relapses, the frequency of nodal involvement is high, but isolated lymph node recurrence (ILNR) is rare. The range spans between 1% and 6%.^{7–9}

ILNR could identify a selected group of patients for whom SCS may be of particular benefit.

The aim of this study is to describe, evaluate and discuss, in the light of the recent literature, feasibility, safety and outcomes of SCS in patient with EOC exclusively relapsed in lymph nodes.

Patients and methods

We conducted a retrospective analysis in five Italian Institutions (University of Torino, National Cancer Institute of Milano, Comprehensive Cancer Centre of Aviano, University of Pisa and National Cancer Institute of Napoli). We selected patients with EOC who underwent secondary cytoreductive surgery for isolated lymph node recurrence in the period between 2000 and 2012. The ILNRs were diagnosed during the scheduled follow-up, including gynecological examination and CA-125 serum measurement every 3 months for the first 2 years and every 6 months thereafter. PET-TC scan, CT or MRI were prescribed in case of clinically suspected recurrence or CA-125 rise.

Inclusion criteria were: history of EOC, good Gynecologic Oncology Group performance status (GOG PS = 0–1), disease free interval (DFI) of at least 6 months from the completion of primary treatments and absence of ascites.

Exclusion criteria were: age >75 years, low Gynecologic Oncology Group performance status (GOG PS = 2), the presence of peritoneal disease and borderline tumor.

Surgical, clinical, pathological and follow-up data were collected. The following characteristics were recorded: age, co-morbidities, FIGO stage, histological type, tumor grade, postoperative residual tumor, type of first line chemotherapy, previous surgery on lymph nodes, DFI from the

completion of primary treatment, sites of nodal recurrence, extent of nodal involvement, residual disease after SCS, hospital stay, postoperative morbidity, post-recurrence progression free survival (PFS), overall survival (OS) after SCS and OS from ovarian cancer diagnosis.

During primary surgery, lymphadenectomy was defined systematic when it was extended to pelvic and para-aortic regions, or partial when it was limited to some retroperitoneal regions or to macroscopically enlarged lymph nodes.

During secondary surgery, median laparotomy and thorough exploration of the abdominal cavity were done. If peritoneal recurrence was detected, the patient was not included in the study. Retroperitoneum was completely explored by sight, palpation and, on the basis of pre-operative imaging, ILNR was identified and resected. All lymph nodes, suspected for metastatic disease on the basis of pre-operative imaging or intra-operative exploration and palpation were removed.

Before surgery, the patient was informed by the surgeon about the treatment, its aims, expected advantages and possible risks. A written consent was signed by patient and surgeon and kept in the personal medical file.

The present retrospective study was submitted and approved by the ethics committee of the Mauriziano Hospital of Torino in compliance with the Helsinki Declaration.

DFI was considered to be the period from the end of primary treatment until the diagnosis of ILNR. PFS after SCS was defined as the period of time from the end of secondary treatment (including post surgical treatments when applicable) until the second recurrence. OS after SCS was considered as the period of time from the end of secondary treatments until either death or the date of the last available follow-up. Global overall survival was considered from the diagnosis of ovarian cancer until either death or the date of the last available follow-up.

Statistical analyses were performed using SPSS 18.0 software (SPSS, Inc., Chicago, IL). Values are presented as median. Estimates of survival were calculated using the Kaplan–Meier method. Log Rank test was adopted to compare differences between survival curves.

Results

We identified and included in the study 73 patients with ILNR who underwent secondary cytoreductive surgery. **Table 1** shows patients characteristics at primary surgery.

At diagnosis, 67 (91.8%) patients received upfront surgery, according to FIGO surgical staging: median laparotomy, complete adhaesiolsysis, total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and resection of all affected organs (small or large bowel, peritoneum, spleen, pancreas tail, liver etc...).¹⁰ The remaining 6 patients (10%) were submitted to interval surgery following neoadjuvant chemotherapy.

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