Prognostic Factors in Patients Undergoing Primary Cytoreductive Surgery for FIGO Stage IIIC Ovarian, Tubal or Peritoneal Cancer

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Abstract

Objective: The aim of the study is to investigate factors related to overall survival in advanced stage ovarian, tubal, or peritoneal cancer and to identify strong and weak prognostic factors.

Methods: We retrospectively reviewed 190 patients who underwent primary cytoreductive surgery between 2003 and 2013.

Results: Median overall survival duration was founded 58 months (95% CI 49–67). Five-year overall survival ratio was 48.5%. Presence of tumour at upper abdomen, suboptimal cytoreduction (residual >1 cm), surgery without lymphadenectomy, and presence of peritoneal ascites more than 1 L had a significantly negative effect on overall survival, but not histological grade and CA-125 level, by univariate Cox analysis. Age and presence of tumour in the upper abdomen were independent poor prognostic factors according to multivariate Cox model (HR 1.025; 95% CI 1.009–1.040 and HR 1.533; 95% CI 1.039–2.263, respectively).

Conclusion: This study supports that the presence of tumour in the upper abdomen is the most important independent poor prognostic factor in patients with performed primary surgery for advanced stage ovarian, tubal, and peritoneal cancer. Upper abdominal metastasis is the most important predictive factor for optimal cytoreduction ($P < 0.001$, HR 6.567; 95% CI 3.059–14.096).

Résumé

Objectif : Le but de la présente étude était d'analyser les facteurs associés à la survie globale chez les patientes atteints d'un cancer de l'ovaire, des trompes ou du péritoine de stade avancé, et de mettre en évidence les facteurs pronostiques forts et faibles.

Méthodologie : Nous avons rétrospectivement examiné le dossier de 190 patientes ayant subi leur chirurgie de réduction tumorale initiale entre 2003 et 2013.

Résultats : La durée médiane de survie globale était de 58 mois (IC à 95 % : 49 à 67), et le taux de survie global après cinq ans était de 48,5 %. Selon une analyse de Cox univariée, la présence d'une tumeur dans l'abdomen supérieur, la cytoréduction sous-optimale (résidu >1 cm), la chirurgie sans lymphadénectomie et la présence d'une ascite de volume supérieur à 1 L avaient une incidence négative significative sur le taux de survie global, mais pas le grade histologique ni le taux de CA 125. Selon un modèle de Cox multivarié, l'âge et la présence d'une tumeur dans l'abdomen supérieur étaient deux facteurs de pronostic péjoratif indépendants (RR : 1,025; IC à 95 % : 1,009 à 1,040; et RR : 1,533; IC à 95 % : 1,039 à 2,263, respectivement).

Conclusion : Cette étude vient confirmer que l'emplacement de la tumeur dans l'abdomen supérieur est le facteur de pronostic péjoratif le plus important chez les patientes ayant subi une chirurgie initiale pour un cancer de l'ovaire, des trompes ou du péritoine de stade avancé. De plus, la présence de métastases dans l'abdomen supérieur est le plus important facteur prédictif de l'efficacité de la cytoréduction optimale ($P < 0,001$; RR : 6,567; IC à 95 % : 3,059 à 14,096).

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INTRODUCTION

Globally, annual ovarian cancer occurs in more than 200 000 women and results in death for more than half.[1,2] More than 95% of ovarian malignancies originate from epithelial cells, a few from other ovarian cell types (germ cell tumours, sex cord stromal tumours).[3] The most common histological subtype is serous (75% of epithelial carcinomas).[3]

Most of the epithelial ovarian malignancies diagnosed at an advanced stage (FIGO stage III or IV) and has a poor overall prognosis. Five-year overall survival rates are around 18% to 32%.[4] Epithelial ovarian carcinoma, fallopian tubes, and peritoneal carcinomas are considered to be a single clinical entity because clinical behaviours and treatments are similar.[5,6]

Cytoreductive surgery followed by a combination chemotherapy consisting of a platinum (carboplatin or cisplatin) plus a taxane is a generally accepted treatment for these patients. Neoadjuvant chemotherapy following by surgery is usually an alternative treatment in patients who are thought to be unsuitable for optimal cytoreduction.

The Gynecologic Oncology Group defines "optimal" as having no residual tumour nodules each measuring more than 1 cm in maximum diameter, and this is most important factor on survival according to current literature.[7–13]

Prognosis of ovarian cancer may be affected by many parameters that may or may not be related to each other, such as age, general performance, surgical performance, stage of the disease, or tumour histology.

In this study, we examined the factors affecting the prognosis of patients with ovarian cancer— those who did not receive neoadjuvant chemotherapy, with stage IIIC, and with epithelial histology. Our aim was to identify strong and weak prognostic factors.

METHODS

For this study, 213 patients who underwent cytoreductive surgery between January 2003 and December 2013 due to advanced ovarian, fallopian tube, or peritoneal cancer at Istanbul University Hospital were examined. Twenty-three patients were excluded from the study. These included six cases of primary appendiceal tumour, one case of primary bile duct tumour, two cases of endodermal sinus tumour, and one case of ovarian lymphoma according to postoperative pathology reports, and 13 patients had missing follow-up. A total of 190 patients were analyzed in this study. The patients were diagnosed with epithelial ovarian cancer were identified by the same gynaecopathologic team. According to the operation reports, all patients had macroscopic metastasis (>2 cm) and omental metastasis.

Patients

At the initial evaluation, a gynaecological exam was performed, tumour markers (CA-125) were assessed, and imaging was performed (mostly MRI, but sometimes CT). The multidisciplinary team, which consisted of gynaecological oncologists, a radiologist, gynaecopathologists, a radiation oncologist, and a medical oncologist, evaluated all patients. The initial diagnosis for patients was either advanced ovarian, fallopian tube, or peritoneal cancer.

In standard debulking procedures, bilateral salpingo-oophorectomy, hysterectomy, appendectomy, or omentectomy were performed, and visible tumours were removed. Pelvic/para-aortic lymphadenectomy or sampling was performed. Other surgical procedures, the most common of which were large/small bowel resection (in 19 patients) and splenectomy (in two patients) were performed when necessary.

Evaluated factors

Age at diagnosis, presence of tumour in the upper abdomen, performance of optimal surgery, pelvic ± para-aortic lymphadenectomy, histological grade of tumour, CA-125 level, and the amount of intra-abdominal ascites were evaluated for overall survival.

Optimal cytoreduction was defined as no macroscopic residual tumour (larger than 1 cm) at the end of the surgical procedure. We obtained this data from the operation report. This information is recorded in the operation report after the surgery.

Upper abdominal metastasis was defined as the presence of a visible tumour on the diaphragm surface or on the liver surface during surgery, according to operation reports.

Levels of CA-125 as a cancer marker were accepted as values determined in pre-treatment examinations (KU/L).

For the ascites data, the total amount of ascites aspirated by the aspirator at the beginning of the laparotomy and deposited in the glass tank was recorded.

Lymphadenectomy was evaluated whether it was applied or not according to operative records and postoperative pathology reports.

Histologic grade of tumour as grade 1–2 or grade 3 was determined according to postoperative pathology reports.

After the operation, all the patients were treated with 6 to 8 cycles of planned chemotherapy. Chemotherapy protocol consisted of a carboplatinum (area under the curves 5–6) and paclitaxel (135–175 mg/m^2) regime every 3 weeks.

The overall survival duration was defined as the time from initial treatment to death or to the last follow-up examination.

Statistical analysis

The Statistical Package for the Social Sciences for Microsoft Windows version 21 (IBM Corporation, NY: USA, 2012) was used to perform all analyses. Survival distributions were estimated by the Kaplan-Meier method. Statistical significance was determined by the log-rank test. The association between survival and survival-related factors was assessed by the Cox proportional hazards model. Evaluation of the presence of tumour in the upper abdomen and related factors was performed using the chi-square test. *P* values less than 0.05 were considered significant for all analyses.