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Original Research

Secondary cytoreductive surgery in recurrent epithelial ovarian cancer: A prognostic analysis with 103 cases

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HIGHLIGHTS

- The relapse rate of epithelial ovarian cancer is high.
- DFI and lesions number were independent prognostic factors for secondary cytoreductive surgery.
- DFI ≥12 months and a single lesion had better prognosis for achieving satisfactory cytoreduction.

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ABSTRACT

Background: Due to satisfactory cytoreductive surgery combined with platinum-based chemotherapy in epithelial ovarian cancer has improved greatly, however, the relapse rate also high. In current study, we analyzed prognostic factors related to secondary cytoreductive surgery in patients with recurrent epithelial ovarian cancer.

Methods: Clinical and follow-up data from 103 patients with recurrent epithelial ovarian cancer who received secondary cytoreductive surgery and were admitted to our hospital between January 2000 and December 2008 were analyzed.

Results: Median survival after recurrence (RS) after the first relapse for the 103 patients was 36 months, and median overall survival (OS) was 60 months. Patients without visible residual tumors after secondary cytoreductive surgery had longer RS and OS compared to those with residual tumors ≥1 cm. The RS and OS of patients without visible residual tumors after secondary cytoreductive surgery were not significantly different compared to those with residual tumors between 0.1 and 1 cm. Patients with disease free interval (DFI) ≥ 12 months at secondary cytoreductive surgery had longer RS and OS compared to those with DFI < 12 months. Patients with one recurrent lesion had longer RS and OS compared to those with more than one lesion.

Conclusions: Residual tumor at secondary cytoreductive surgery, DFI and number of lesions were independent prognostic factors for secondary cytoreductive surgery in patients with epithelial ovarian cancer. Patients with DFI ≥12 months and a single lesion had better prognosis for achieving satisfactory cytoreduction, especially the absence of visible residual tumors.

1. Introduction

Epithelial ovarian cancer is one of the common gynecological malignancies. The five-year survival rate in epithelial ovarian cancer has improved greatly due to satisfactory cytoreductive surgery combined with platinum-based chemotherapy. However, even after systemic treatment involving surgery with chemotherapy, the relapse rate at the early stages of epithelial ovarian cancer is still 20%–25%, while that at the advanced stages can be as high as 70% [1]. The treatment procedure after relapse is mainly chemotherapy, although surgery can also be performed on a proportion of patients. Reports on the prognosis of patients with recurrent epithelial ovarian cancer who underwent secondary cytoreductive surgery are inconsistent. In this study, a total of 103 patients from our hospital with recurrent epithelial ovarian cancer who underwent secondary cytoreductive surgery were included. Their surgical

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conditions were analyzed retrospectively, including clinical and pathological data, recurrence condition, and conditions of secondary surgery, in order to explore the factors related to the prognosis of patients with recurrent epithelial ovarian cancer who underwent secondary cytoreductive surgery.

2. Methods

2.1. Basic information

A total of 103 patients with recurrent epithelial ovarian cancer, who received secondary cytoreductive surgery and were admitted to the Department of Gynecology at the Fourth Hospital of Hebei Medical University between January 2000 and December 2008, were selected as subjects for this study. Detailed records were kept, which included the age of onset, condition of residual tumor after the first surgery, tumor pathology, pathological staging, recurrence conditions, and conditions of secondary surgery. All patients underwent surgery and 6–8 courses of platinum-based adjuvant chemotherapy for their first treatment, as well as secondary cytoreductive surgery after relapse followed by systemic adjuvant chemotherapy. Responders (platinum-sensitive) were defined as an ovarian cancer patient who had a treatment-free interval greater than 6 months from the last date of the initial six cycles of platinum-based combination chemotherapy. A nonresponder (platinum-resistance) was defined as an ovarian cancer patient who had a treatment-free interval less than 6 months from the last date of the initial six cycles of platinum-based combination chemotherapy, including disease that had progressed during chemotherapy. All patients were followed-up until October 2012.

2.2. Conditions of secondary surgery

All 103 patients underwent surgery for their first treatment and after recurrence, which was followed by adjuvant chemotherapy. Selection of patients with recurrent epithelial ovarian cancer, DFI $\geq$12 months and a single lesion, as well as achieving satisfactory cytoreduction or even removing all visible residual tumors as much as possible. Based on the condition of residual tumor during surgery, patients were divided into groups: no visible residual tumor, residual tumor with diameter <1 cm and residual tumor with diameter $\geq$1 cm, whereby residual tumor <1 cm was classified as satisfactory cytoreduction.

2.3. Disease free interval, survival after recurrence and overall survival

DFI refers to the interval between the day of the last chemotherapy treatment and disease relapse. Based on the treatment-free interval before secondary cytoreductive surgery, patients were divided into two groups: treatment-free interval $\geq$12 months and treatment-free interval <12 months. RS refers to the interval between the day of recurrence diagnosis and death or the last follow-up. OS refers to the interval between the day of diagnosis and death or the last follow-up.

2.4. Statistical analysis

Measurement data were described using median, mean and standard deviation. Count data were described using ratio and percentage. SPSS 19.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. Survival times were analyzed using Kaplan-Meier estimator and Cox regression model; differences were tested using the Log-rank test. $P < 0.05$ indicated statistical significance.

3. Results

3.1. Basic patient information at first treatment

As shown in Table 1, the median age of the 103 patients at disease onset was 49 years old, of which the youngest was 29 years old and the oldest was 74 years old. At the end of follow-up, 68.9% (71/103) had died and 31.1% (32/103) survived; OS was 20–114 months, and the median OS was 60 months.

3.2. Conditions at secondary cytoreductive surgery after relapse

As shown in Table 2, the median RS of the 103 patients after the first relapse was 36 months. During secondary cytoreductive surgery, nine patients underwent splenectomy, eight underwent partial hepatectomy, four underwent Dixon's operation, 24 underwent small intestine or colon resection, seven underwent intestinal fistula, 13 underwent pelvic and/or para-aortic lymph node biopsy or dissection, and the remaining cases underwent abdominal cytoreductive surgery.

3.3. Univariate analysis of factors influencing RS and OS

Using RS and OS as the dependent variables, univariate analyses were conducted to examine various factors that might have influenced the patients' RS and OS (Table 3). Univariate analysis of age, pathology type, differentiation degree, residual tumor at first surgery, chemotherapy before cytoreductive surgery, CA-125 before secondary cytoreductive surgery, ascites before secondary cytoreductive surgery and maximum size of lesion at relapse did not reveal clear correlations with RS and OS. FIGO stage, DFI at secondary cytoreductive surgery, number of lesions at relapse and residual tumor at secondary cytoreductive surgery were correlated with the patients' RS and OS.

3.4. Multivariate Cox regression analysis

Univariate analysis revealed that FIGO stage was correlated with patients' RS and OS. However, multivariate analysis did not show statistical significance, which may due to a small number of stage I

Table 1
Basic patient information at first treatment.

	Cases	Percentage (%)
Residual tumor at first surgery		
No residual tumor	35	34.0
≤1 cm	40	38.8
>1 cm	28	27.2
Pathological stage		
I	5	4.90
II	29	28.1
III	61	59.2
IV	8	7.80
Pathological type		
Mucinous adenocarcinoma	16	15.5
Serous adenocarcinoma	75	72.8
Other epithelial cancers[a]	12	11.7
Degree of differentiation		
High differentiation	3	2.9
Moderate differentiation	16	15.6
Low differentiation	71	68.9
Differentiation not recorded	13	12.6

FIGO: International Federation of Gynecology and Obstetrics.
[a] Including one case of mucinous adenocarcinoma, two cases of clear-cell carcinoma, four cases of endometrial adenocarcinoma, one case of transitional cell carcinoma and four cases of mixed epithelial carcinoma.