

# Outcomes of conservative surgery in early epithelial ovarian carcinoma

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## Summary

**Objective:** To investigate clinical outcomes and fertility status of conservative treatment for epithelial ovarian carcinoma. **Methods:** The data of clinicopathological characteristics and follow-up were retrospectively collected and analyzed in 17 patients with early epithelial ovarian carcinoma who underwent conservative surgery. **Results:** The tumor histologic types of 17 patients included 13 mucinous, one serous, one endometrioid, and two mixed mucinous and serous carcinomas. The FIGO stages were: ten Stage IA, six IC, and one IIIA disease. Tumor grades involved 15 grade 1 and two grade 2. Sixteen patients received adjuvant platinum-based combined chemotherapy. The medium duration of follow-up was 61 months (range 17~115 months). Only one patient recurred at 36 months after primary surgery. All of the 17 patients were alive at end of follow-up. Eight patients attempted pregnancy and five patients conceived naturally; there were six term pregnancies and one abortion. **Conclusion:** Conservative surgery can be considered for young patients with FIGO Stage I including grade 1 and grade 2 epithelial ovarian cancers who desire further childbearing.

**Key words:** Epithelial ovarian carcinoma; Conservative surgery; Recurrence; Pregnancy.

## Introduction

Epithelial ovarian carcinoma is the most common histological type in ovarian malignancies. Although 80% of epithelial ovarian carcinomas are found in postmenopausal women, they do occur in women in reproductive age as well. The 25<sup>th</sup> FIGO Annual Report showed that about 14% of epithelial ovarian carcinomas would occur in women younger than 40 years, and 62% of ovarian cancers diagnosed before 40 years would be at Stage I-IIA [1].

Surgery is the cornerstone of treatment for epithelial ovarian carcinoma. The standard surgical treatment for early-stage epithelial ovarian carcinoma includes hysterectomy with bilateral salpingo-oophorectomy, omentectomy, peritoneal sampling, lymph node sampling, and peritoneal washing for cytology, with or without appendectomy. However radical surgery means loss of fertility in those young patients who wish childbearing. In order to preserve fertility in young patients, an operation to preserve the uterus and contralateral ovary has been proposed for selected epithelial ovarian carcinoma patients. As early as 1969, Munnell [2] reported 190 cases of unilateral epithelial or nonepithelial ovarian cancer treated at his institution. The age range of women was 20 to 77. The 5-year survival was 79% for the patients operated radically and 74% for those conservatively. The reports about conservative surgery for epithelial ovarian carcinoma have accumulated in the past decade, but most were from European and American populations [3-14]. Indications of conservative surgery for epithelial ovarian carcinoma are not still uniform, and clinical outcomes and fertility status following surgery were discrepant as well.

The aim of this study was to investigate clinical outcomes and fertility results of conservative surgery for early epithelial ovarian carcinoma cases to provide evidence of an available management strategy for young patients.

## Materials and Methods

Between 1999 and 2007, a total of 17 patients with primary epithelial ovarian carcinoma underwent conservative surgery in the Department of Gynecologic Oncology, Women's Hospital, School of Medicine, Zhejiang University, China. Histology diagnoses were reconfirmed by an experienced pathologist in the Department of Pathology. Histology was classified by the World Health Organization (WHO, 1999) criteria and tumor grade was defined by the classification of Shimizu *et al.* (2000) [15]. Tumors were staged according to the Federation of Gynecology and Obstetrics staging system (FIGO, 1988).

Clinicopathological characteristics, including the age of patients, tumor histology and differentiation, clinical stage, surgery, adjuvant chemotherapy, survival status, menstruation and pregnancy after surgery of 17 patients treated with conservative surgery were reviewed and collected. The information was obtained from medical records and telephone interviews. Follow-up for the patients after surgery included physical examination, serum CA125 testing and an ultrasonographic (US) scan every two months during the first year, then every three months for two years, then every six months for two years, and yearly afterward.

## Results

### Patient characteristics

The mean age of 17 patients at the time of surgical procedure was 23.2 years (range 16-30 years). All of the patients were nulliparous. Seventeen tumor histologic types included 13 (76%) mucinous carcinomas: one (6%) serous, one (6%) endometrioid, and two (12%) mixed

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mucinous and serous. Ten (59%) patients were FIGO Stage IA, six (35%) IC, and one (6%) IIIA. Tumor grade was grade 1 in 15 (88%) and two (12%) were grade 2. Clinicopathological characteristics of all patients are summarized in Table 1.

All the patients underwent conservative primary operations with complete surgical staging, including multiple washing for cytology, diaphragmatic smearing, unilateral salpingo-oophorectomy, omentectomy, peritoneal sampling, retroperitoneal lymph node sampling, and appendectomy for mucinous or mixed histologic subtype. Five patients who had contralateral ovarian tumors or cysts underwent tumor resection or cystectomy; of those, three were pathologically confirmed as benign tumors and two as borderline tumors. Three patients with a normal appearing contralateral ovary underwent biopsy and all pathological diagnoses were normal.

Totally 16 patients received 3.8 (range 2-6) courses of adjuvant platinum-based combined chemotherapy, except for one patient with Stage IA and grade 1. Chemotherapy regimens were paclitaxel (175 mg/m<sup>2</sup>) and carboplatin (AUC=5) or carboplatin (AUC=5) and cyclophosphamide (600 mg/m<sup>2</sup>) (Table 2).

#### Recurrence and survival

The patients were followed-up for 61 months (17~115). All 17 patients were alive until the end of follow-up. Sixteen patients were disease-free during the follow-up period. One patient with Stage IC, grade 1, and mixed serous and mucinous carcinoma recurred in the rectouterine pouch and left iliac lymph node 36 months after the primary surgery. She underwent hysterectomy, appendectomy, and tumor resection. The second debulking surgery was optimal with no gross residual tumor. The histological type was the same as for the first surgery, but tumor grade was grade 2. She received a further six courses of paclitaxel and carboplatin chemotherapy and was alive without any evidence of disease six months after the end of chemotherapy.

#### Ovarian endocrine function and fertility results

Of the 16 patients treated by chemotherapy, 15 had regular menses as before. Only one patient who had undergone unilateral salpingo-oophorectomy and contralateral ovarian cystectomy complained of temporary menopause during three courses of chemotherapy. Her menstruation restarted two months later but the cycle was longer and flow decreased.

Among 16 disease-free patients, eight attempted pregnancy. Of those, five conceived naturally and totally there were six term babies and one abortion. Another three patients were infertile, but the reasons were unclear. No congenital malformations were found in any of the offspring.

#### Discussion

In general, epithelial ovarian carcinoma is a disease of postmenopausal women, but has been documented to occur in young women for whom preservation of fertility

Table 1. — Clinicopathological characteristics of 17 patients with epithelial ovarian carcinoma who underwent conservative surgery.

Clinical characteristics	Number (%)
Patient age	23.2 (16~30) years
Histologic type	
Mucinous	13 (76%)
Serous	1 (6%)
Endometrioid	1 (6%)
Mixed	2 (12%)
FIGO stage	
IA	10 (59%)
IC	6 (35%)
IIIA	1 (6%)
Grading	
G1	15 (88%)
G2	2 (12%)

Table 2. — Adjuvant chemotherapy for 16 patients.

FIGO stage and tumor grade	No. of patients	Paclitaxel + carboplatin	Carboplatin + cyclophosphamide
Stage IA			
Grade 1	8	3	5
Grade 2	1	0	1
Stage IC			
Grade 1	5	2	3
Grade 2	1	1	0
Stage IIIA			
Grade 1	1	1	0
Total	16	7	9

needs to be clinically considered. It is widely accepted that fertility-sparing surgery can be applied in FIGO Stage IA and grade 1 tumors. However, some studies revealed that conservative management was probably available for those beyond this phase of disease in the past more than ten years. Zanetta *et al.* [3] reported 99 young patients with Stage I ovarian carcinomas. Of those, 56 including 24 higher than Stage IA and 22 higher than grade 1 underwent fertility-sparing surgery and 43 patients with similar stage and grade underwent radical surgery. With a median follow-up of seven years, five (9%) women treated conservatively had recurrence and five (12%) of those treated radically. Similarly, Schilder *et al.* [4] reported a total of 52 patients treated by fertility-sparing surgery, who were composed of 42 Stage IA and ten Stage IC diseases that included 38 grade 1, nine-grade 2, and five grade 3 tumors. The estimated survival was 98% at five years and 93% at ten years. Furthermore, Raspagliesi *et al.* [5] reported ten high-risk epithelial ovarian carcinoma patients who underwent conservative surgery, including two Stage IA/grade 3; two Stage IC; two Stage IIIA; and four Stage IIIC diseases. All patients were alive and disease-free at a medium of 70 months of follow-up period, suggesting fertility-sparing surgery may be also available for some women with higher than Stage I, grade 2 epithelial ovarian cancer. However, this opinion is still debated. Morice *et al.* [6, 7] reported 25 patients treated by conservative surgery, including 19 Stage IA (9 grade 1 and 10 grade 2), one Stage IC, two

Stage 2, and three unknown stage diseases. At the medium 47 months of follow-up, three Stage IA and all Stage IC or higher patients recurred, and three of them died. Four years later, they conducted a multicenter study on 34 patients with epithelial ovarian carcinoma treated conservatively. Seven patients with Stage IA disease (2 grade 1, 4 grade 2, and 1 grade 3) and four with Stage IC or higher disease experienced recurrence, and four died at a medium of 47 months of follow-up. Thus, their results indicated that conservative surgery should not be considered for patients staged higher than FIGO Stage IA.

In our study, 17 patients with early epithelial ovarian carcinoma, including ten FIGO Stage IA, six Stage IC, and one Stage IIIA, as well as 15 grade 1 and 2 grade 2, underwent conservative surgery. All of 17 patients were alive and 16 were disease-free during a medium of 61 months of follow-up. Only one Stage IC patient recurred at 36 months after primary surgery but still survived till the follow-up end. Ours and other investigations indicate that conservative surgery can be considered for young patients with FIGO Stage I including grade 1 and grade 2 epithelial ovarian cancer who desire further childbearing, but caution is necessary if this surgical procedure is planned for those with higher than Stage I or grade 3 disease.

Complete surgical staging should be performed during conservative surgery to exclude the presence of occult extraovarian disease. The incidence of microscopic implants in a gross normal appearing ovary was not consistent among different series. It was estimated there was a 12% risk for microscopic carcinoma on the contralateral normal appearing ovary [2], but only 2.5% (3/118) of occult contralateral ovarian involvement was found in Stage I epithelial ovarian carcinoma in a recent report [16]. We did not find microscopic metastasis by biopsy in three normal appearing ovaries, like a previous study [3]. In addition, since ovary biopsy may induce adhesion and subsequent infertility, this procedure is not advisable for a normal appearing ovary.

It is generally believed that fertility potential is not obviously decreased in women who undergo conservative surgery for ovarian cancer. Zanetta *et al.* [3] reported 27 pregnancies in 20 patients treated conservatively. Schilder *et al.* [4] reported that 17 patients conceived and had 26 term deliveries and five spontaneous abortions in 24 patients who attempted pregnancy, and Park *et al.* [8] reported 22 term pregnancies in 19 women attempting to conceive. However, Morice *et al.* [6] showed that only four patients had four pregnancies among 18 disease-free patients. In our data, five women conceived spontaneously in eight attempting pregnancy, and no congenital malformations of the babies were found. Our data suggest that conservative surgery is an effective procedure for women with ovarian cancer who desire childbearing.

It remains controversial whether hysterectomy and contralateral salpingo-oophorectomy should be performed after completion of childbearing. Since the remaining ovary contributes to maintenance of endocrine function, radical surgery is no longer performed for young women in many institutions. Based on our and others follow-up data [8], the remaining ovaries after

conservative surgery on the whole have long-term survival. It may be acceptable, just as suggested by Colombo *et al.* [16], that in any case the final choice should be individualized and risk factors of relapse should be taken into consideration.

In conclusion, conservative surgery can be considered for young patients with FIGO Stage I, including grade 1 and grade 2 epithelial ovarian cancers, who desire further childbearing.

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