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CLINICAL ARTICLE

Pregnancy after fertility-sparing surgery for borderline ovarian tumors

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ABSTRACT

Objective: To investigate the ability to conceive and the factors affecting chances of pregnancy among patients with borderline ovarian tumors (BOTs) treated with fertility-sparing surgery. *Methods:* A retrospective study included nulliparous patients aged 40 years or younger who had undergone fertility-sparing surgery for BOTs between January 2005 and June 2012 at a center in Fuzhou, China. Identified patients were followed up by telephone or mail between March 15 and June 30, 2013. Patients who had already been pregnant and those who had not but had discontinued contraception for more than 1 year were included in final analyses. *Results:* Among 23 included patients, 17 (74%) had become pregnant within the mean follow-up period of 48.2 months. The frequencies of previous infertility, sequelae of pelvic inflammatory disease, and endometriosis were all higher in the nonpregnant group than in the pregnant group ($P \le 0.021$ for all). More women in the nonpregnant group that in the pregnant group had BOTs of stage II or worse, but the difference was nonsignificant ($P = 0.059$). *Conclusion:* Fertility-sparing surgery in young patients with BOTs is associated with a good pregnancy rate. However, the tumor stage and coexisting infertility factors are important considerations in selecting the optimal surgical approach.

1. Introduction

Borderline ovarian tumors (BOTs) are a subgroup of epithelial ovarian tumors with histopathologic features and a biological behavior intermediate between clearly benign and frankly malignant [1,2]. By contrast with invasive carcinoma, BOTs grow slowly and mostly carry a favorable prognosis. At diagnosis, approximately 75% of BOTs are at International Federation of Gynecology and Obstetrics (FIGO) stage I [3]. The 5-year and 10-year survival rates for women with stage I BOTs are very favorable—approximately 95%–97% and 70%–95%, respectively [4]. Even if diagnosed at a more advanced stage (stages II–III), the 5-year survival rate can still reach 65%–87% [4].

With the peak incidence occurring at reproductive age, most BOTs are diagnosed in women aged between 20 and 40 years. The mean age at diagnosis is approximately 10 years younger than that of women with invasive ovarian carcinoma [5]. Understandably, many patients with BOTs wish to undergo treatments that will allow them to retain fertility. Therefore, fertility-sparing surgical treatment has been recommended for young patients with stage I BOTs who want to preserve their childbearing potential [6]. Some studies [7,8] have shown that conservative surgery can also be performed for women with BOTs of higher stages who wish to preserve their fertility.

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A main concern about fertility-sparing surgery for BOTs is whether it will increase the risk of tumor recurrence and thus reduce patient survival. One large study [9] showed that fertility-sparing surgery did not affect the patient survival rate: the rate of BOT recurrence after fertility-sparing surgery was higher than that after radical surgery, but there was no difference in the survival rate. In fact, the disease-free survival rate reached 99.3% among patients who underwent fertility-sparing surgery for stage I BOTs. Furthermore, a multicenter, retrospective study [10] of data for 360 patients in France who were treated between 1990 and 2000 found no differences in the tumor recurrence rate and the mean time to recurrence between women who became pregnant and those who did not.

The pregnancies achieved in patients undergoing fertility-sparing surgery for BOTs and the factors influencing the chances of pregnancy are a matter of much interest. In a systematic review [11], the pregnancy rate after conservative treatment of early-stage BOTs was 54%. The age at diagnosis seems to have a strong influence on postsurgical fertility: the pregnancy rate of women with BOTs who were older than 40 years was greatly reduced in the French multicenter study [10]. For patients with infertility after surgery, assisted reproductive technology can help to achieve a pregnancy, but ultraconservative surgery might increase the risk of tumor recurrence [11]. The pooled pregnancy rate after in vitro fertilization in the systematic review [11] was 80%; the tumor recurrence rate was 23%, which was still considered to be "low."

Morice et al. [12] showed that for patients with unilateral BOTs, unilateral salpingo-oophorectomy can preserve good reproductive

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capabilities, with the tumor recurrence rate being lower than after unilateral cystectomy. Therefore, studies tend to recommend unilateral salpingo-oophorectomy for young patients with unilateral BOTs who wish to preserve their fertility [12,13]. As for patients with bilateral BOTs, a randomized, controlled study by Palomba et al. [6] showed that bilateral cystectomy not only resulted in a higher pregnancy rate than unilateral salpingo-oophorectomy and contralateral cystectomy, but it also shortened the time to conception. An extension study by the same authors [14] further supported these findings. However, they found that the basal level of follicle-stimulating hormone in patients undergoing unilateral salpingo-oophorectomy and contralateral cystectomy increased earlier and more prominently than that in patients undergoing bilateral cystectomy [14].

Previous research has focused on the rate of recurrence and survival after fertility-sparing surgery for BOTs. However, little is known in China regarding the determinants of fertility in this setting. The aim of the present study was to investigate the ability to conceive and the factors affecting the achievement of pregnancy among young patients with BOTs who wished to get pregnant and were treated with fertility-sparing surgery.

2. Materials and methods

In a retrospective study, data were reviewed for all patients with BOTs who had undergone fertility-sparing treatment in the Department of Obstetrics and Gynecology at Fujian Maternity and Children Health Hospital in Fuzhou, China, between January 1, 2005, and June 30, 2012. Nulliparous patients who were no older than 40 years were retrospectively identified. Because this was a retrospective study, institutional review board approval was waived. Patients provided consent for inclusion at the time of follow-up.

The pathologic diagnosis of BOT had been made according to the WHO histologic classification of ovarian tumor types [15]. The tumor stage was defined according to the FIGO criteria for epithelial ovarian cancer [16]. Surgery was the primary treatment. Fertility-sparing surgery was defined as a procedure in which the uterus and at least a portion of one ovary were preserved [7]. Four types of conservative surgical procedure were performed: unilateral salpingo-oophorectomy, unilateral salpingo-oophorectomy with contralateral cystectomy, unilateral cystectomy, and bilateral cystectomy [8].

Identified patients were followed up by telephone or mail between March 15 and June 30, 2013. Patients who were followed up and completed a questionnaire designed for the study were included in final analyses. All women who had delivered or been pregnant since surgery were included. Women who had not delivered or been pregnant were included only if they had discontinued contraception for more than 1 year by the time of follow-up.

The questionnaire obtained information about current health status, frequency of intercourse, contraception, and pregnancy. The patients were divided into two groups on the basis of whether they had become pregnant between surgery and follow-up. The data were processed using SPSS version 18.0 (SPSS Inc, Chicago, IL, USA). Quantitative variables were analyzed using one-way analysis of variance, and categorical variables were analyzed using the χ^2 or Fisher exact test as appropriate. $P < 0.05$ was considered statistically significant.

3. Results

Of 38 patients identified, 34 were contacted successfully by telephone or postal mail. Of the 34 patients with successful follow-up, 11 patients were excluded from the study: eight were single and had no fertility requirement, two were married but had not discontinued contraception at least 1 year previously, and one was found to be pregnant (16 weeks) during surgery and thus had ovarian cystectomy followed by an uneventful full-term delivery. The remaining 23 patients were included in the final analysis.

Among the 23 patients, the age at diagnosis ranged from 17 to 32 years, with a median age of 27 years and a mean age of 26.7 years. Nineteen patients were aged 30 years or younger, whereas the remaining four patients were aged 30–32 years old; no patient was older than 32 years.

The BOTs in the 23 patients were classified as serous borderline papillary cystadenoma (n = 11), mucinous borderline tumor (n = 7), borderline mixed epithelial tumor (n = 3), and mucinous borderline papillary cystadenoma (n = 2). The tumor stage was classified as stage IA in 16 patients, stage IB in two patients, stage IC in three patients, stage IIC in one patient, and stage IIIB in one patient.

Over a follow-up duration of 14–96 months (mean 48.2), 17 of the 23 patients had become pregnant (pregnancy rate 74%); all these women conceived naturally. The remaining six patients did not conceive. In the pregnant group, the mean time from primary treatment to first conception was 13 months (range 1–48). In the nonpregnant group, the mean time from primary treatment to follow-up was 23.5 months (range 14–60).

In the pregnant group, the mean time from discontinuation of contraception to first conception was 6 months (range 1–15), and 14 (82%) of the 17 patients conceived within 1 year of attempting to become pregnant. By contrast, in the nonpregnant group, the mean time from discontinuation of contraception to follow-up was 22.5 months (range 13–59). The difference between the time from discontinuation of contraception to conception in the pregnant group and the time from discontinuation of contraception to follow-up in the nonpregnant group was significant ($P < 0.001$).

In the nonpregnant group, five of six patients had previously been infertile, whereas only one of the 17 patients in the pregnant group had been infertile ($P = 0.001$) (Table 1). The identification of sequelae of pelvic inflammatory disease was more common in the nonpregnant group than in the pregnant group ($P = 0.008$) (Table 1). The difference in the frequency of endometriosis found during surgery was also significant ($P = 0.021$) (Table 1).

With regard to tumor stage, in the nonpregnant group, three patients had a stage IA tumor, one had a stage IC tumor, one had a stage IIC tumor, and one had a stage IIIB tumor. In the pregnant group, 13 patients had a stage IA tumor, two had a stage IB tumor, and two had a stage IC tumor.

Table 1
Characteristics of patients by subsequent pregnancy status.

Characteristic	Pregnant group (n = 17)	Nonpregnant group (n = 6)	*P* value
Previous infertility			0.001
Yes	1	5	
No	16	1	
Surgical approach			0.621
Open	12	3	
Laparoscopic	5	3	
Type of surgery			0.279
Unilateral salpingo-oophorectomy/ unilateral cystectomy	14	3	
Unilateral salpingo-oophorectomy and contralateral cystectomy/bilateral cystectomy	3	3	
Sequelae of pelvic inflammatory disease[a]			0.008
Yes	1	4	
No	16	2	
Endometriosis			0.021
Yes	2	4	
No	15	2	
FIGO stage			0.059
I	17	4	
>I	0	2	
Chemotherapy			>0.99
Yes	4	1	
No	13	5	

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.
[a] Fallopian tube adhesions, tubal thickening, fimbrial atresia, and hydrosalpinx.