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CLINICAL ARTICLE

Outcomes of fertility-sparing surgery among young women with FIGO stage I clear cell carcinoma of the ovary

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ABSTRACT

Objectives: To evaluate the outcome of fertility-sparing surgery among young women with early-stage clear cell carcinoma of the ovary. *Methods:* In a retrospective study, data were reviewed for patients aged 45 years or younger who had FIGO stage I clear cell carcinoma of the ovary and had attended one institution in South Korea between December 1999 and December 2009. Outcomes were compared between women undergoing fertility-sparing surgery, defined as preservation of the uterus and at least one adnexa, and those undergoing radical surgery. *Results:* Overall, 47 patients were included (22 underwent fertility-sparing surgery, 25 radical surgery). After a median follow-up of 72 months (range 8–175), 5 (23%) patients who underwent fertility-sparing surgery and 5 (20%) in the radical surgery group had recurrent disease ($P = 0.820$). The mean time to recurrence was 19 months after fertility-sparing surgery versus 20 months after radical surgery ($P = 0.935$). The anatomical location of recurrence did not differ. There was no difference in 5-year disease-free survival (77% vs 84%; $P = 0.849$) or 5-year overall survival (91% vs 88%; $P = 0.480$). *Conclusion:* Fertility-sparing surgery was found to be a safe alternative for young women with FIGO stage I clear cell carcinoma of the ovary who wish to preserve fertility.

1. Introduction

Ovarian cancer is the second most common gynecologic cancer and a leading cause of cancer-related death in the USA [1]. Similarly, it is the third most common gynecologic cancer and a leading cause of death due to cancer in South Korea [2,3]. Epithelial ovarian cancer accounts for more than 95% of all ovarian cancers [4]. Clear cell carcinoma of the ovary is a fairly rare histologic type of epithelial ovarian cancer. Substantial geographic variation in its prevalence has been recorded: it accounts for approximately 1%–12% of all epithelial ovarian cancer in North America and Europe, but more than 25% in Japan [5–7].

The standard surgical management of epithelial ovarian cancer includes total hysterectomy and bilateral salpingo-oophorectomy [8]. However, fertility-sparing surgery has been proposed as a safe alternative for selected young women with early-stage epithelial ovarian cancer who wish to preserve their fertility [9–13]. Retrospective studies suggest that fertility-sparing surgery can be performed safely for patients with International Federation of Gynecology and Obstetrics (FIGO) stage IA and IC epithelial ovarian cancer, although there has not been a prospective trial [14]. However, most studies have examined the safety of fertility-sparing surgery for serous adenocarcinoma of the ovary rather than clear cell carcinoma, owing to the rarity of the latter. Nevertheless, because clear cell carcinoma is usually diagnosed as an early-stage disease among young women with endometriosis or during fertility treatment, the need for fertility-sparing surgery is very high [15,16]. Two retrospective studies have specifically addressed fertility-sparing surgery among young women with early-stage clear cell carcinoma of the ovary, but were limited by their sample sizes of only 30 [9] and 16 [17,18].

The aim of the present study was to evaluate the outcomes of fertility-sparing surgery among young women with early-stage clear cell carcinoma of the ovary by comparing them with those of radical surgery.

2. Materials and methods

In a retrospective single-center study, data were reviewed from patients with FIGO stage I clear cell carcinoma of the ovary who had been treated and followed up at Asan Medical Center (AMC), Seoul, South Korea, between December 1, 1996, and December 31, 2009. Eligible patients were aged 45 years or younger. Approval for the study was obtained from the Institutional Review Board of AMC.

Clinicopathologic data were extracted for age, parity, comorbid medical disease, history of previous abdominal surgery, preoperative serum cancer antigen 125 (CA125) level, surgical procedures, surgery mode, restaging, fertility-sparing surgery, histology, ovarian tumor size, ovarian surface involvement, tumor rupture, peritoneal cytology, FIGO stage, adjuvant chemotherapy, recurrence, anatomical site of the

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recurrent disease, time to recurrence, follow-up duration, and patient status at the last follow-up. The study patients were divided into two groups on the basis of the type of surgery: fertility-sparing surgery was defined as the preservation of the uterus and at least one adnexa; radical surgery was defined as the removal of the uterus and both adnexa. Clinicopathologic characteristics and survival outcomes were compared between the two groups.

Statistical analyses were performed with SPSS version 21.0 (IBM, Armonk, NY, USA). Mean values were compared by Student *t* test or Mann–Whitney *U* test, and frequency distributions were compared by χ^2 test or Fisher exact test. Disease-free survival time was defined as the time, in months, from the date of surgery to the date of recurrence, date of last follow-up, or censored date. The overall survival time was defined as the time, in months, from the date of surgery to the date of death, date of last follow-up, or censored date. Survival curves were calculated by the Kaplan–Meier method and the survival difference was compared by a log-rank test or Cox proportional hazard model. $P < 0.05$ was regarded as statistically significant.

3. Results

During the study period, 149 patients with clear cell carcinoma of the ovary were treated and followed up at AMC. Among these patients, 47 met the inclusion criteria for the study and were included in the analysis. From the final pathology reports, no patients had microscopic lymph node metastasis: the clear cell carcinoma was found to be confined to the ovary during surgery. The mean age was 38.8 ± 4.7 years (range 28–45).

Among the 47 study patients, 22 underwent fertility-sparing surgery and 25 underwent radical surgery as their primary surgical treatment. Patients who underwent fertility-sparing surgery were significantly younger than were those who underwent radical surgery ($P = 0.001$) (Table 1). More patients in the radical surgery group had a history of abdominal surgery ($P = 0.010$) and a parity of at least one ($P < 0.001$), but no other significant differences in characteristics were recorded (Table 1).

All patients underwent a staging operation, including peritoneal exploration, cytology, and biopsy sampling at AMC. Overall, 9 (41%) patients in the fertility-sparing surgery group and 7 (28%) patients in the radical surgery group underwent a restaging operation at AMC after incomplete surgery at another hospital ($P = 0.351$), and 9 (41%) and 5 (20%) patients, respectively, underwent a staging operation via laparoscopy ($P = 0.118$). The frequencies of pelvic and para-aortic lymphadenectomy did not differ between groups ($P = 0.654$) (Table 2). Omentectomy was also performed for similar numbers of patients in both groups ($P > 0.99$) (Table 2).

In the fertility-sparing surgery group, all patients underwent unilateral salpingo-oophorectomy as the fertility-sparing surgical procedure (Table 2). Seven underwent cystectomy of the contralateral ovary, although they did not have carcinoma of the contralateral ovary. Overall, ovarian endometriosis was found in 31 (66%) patients; however, no patient required low anterior resection to remove coexisting endometriosis.

After completion of treatment, patients were followed up at 3-month intervals for 2 years, 6-month intervals for the next 3 years, and then yearly thereafter. The median follow-up duration of all patients was 72 months (range 8–175). There was no difference in follow-up duration between the fertility-sparing surgery group (82 months, range 23–175) and the radical surgery group (77 months, range 8–160; $P = 0.672$). Recurrent disease was noted in 5 (23%) patients in the fertility-sparing surgery group and 5 (20%) patients in the radical surgery group ($P = 0.820$). Table 3 shows the characteristics of patients who had recurrent disease. The mean time to recurrence was 19 months in the fertility-sparing surgery group and 20 months in the radical surgery group ($P = 0.935$). The anatomical location of recurrence did not differ between the two groups. Four (18%) patients who underwent fertility-sparing surgery and 2 (8%) patients who underwent radical surgery died from the disease ($P = 0.670$).

The 5-year disease-free survival and overall survival of all patients were 81% and 89%, respectively. There was no difference in 5-year

Table 1
Characteristics of the study patients by type of surgery.[a]

Characteristics	Fertility-sparing surgery (n = 22)	Radical surgery (n = 25)	*P* value
Age, y	36.5 ± 4.9	40.9 ± 3.6	0.001
≤ 38	13 (59.1)	7 (28)	0.031
> 38	9 (40.9)	18 (72)	
Parity			
0	19 (86)	8 (32)	<0.001
≥ 1	3 (14)	17 (68)	
Comorbidity			
No	21 (96)	22 (88)	0.611
Yes	1 (4)	3 (12)	
Previous abdominal surgery			
No	20 (91)	14 (56)	0.010
Yes	2 (9)	11 (44)	
Restaging			
No	13 (59)	18 (72)	0.351
Yes	9 (41)	7 (28)	
Preoperative serum CA125, U/mL	66.2 ± 89.2	55.9 ± 71.6	0.662
≤ 60	15 (68)	20 (80)	0.354
> 60	7 (32)	5 (20)	
Surgery mode			
Laparotomy	13 (59)	20 (80)	0.118
Laparoscopy	9 (41)	5 (20)	
Histology			
Pure clear cell carcinoma	19 (86)	24 (96)	0.328
Mixed clear cell carcinoma	3 (14)	1 (4)	
Tumor size, cm	9.9 ± 6.2	8.3 ± 4.8	0.328
≤ 9	9 (41)	16 (64)	0.113
> 9	13 (59)	9 (36)	
Intraoperative rupture			
No	18 (82)	16 (64)	0.207
Yes	4 (18)	9 (36)	
Peritoneal cytology			
No	22 (100)	23 (92)	0.491
Yes	0 (0)	2 (8)	
Ovarian surface involvement			
No	19 (86)	19 (76)	0.470
Yes	3 (14)	6 (24)	
FIGO stage			
IA	12 (55)	10 (40)	0.319
IC	10 (45)	15 (60)	
Adjuvant chemotherapy			
No	2 (9)	2 (8)	>0.99
Yes	20 (91)	23 (92)	
Chemotherapy regimen[b]			
Taxane + platinum	16 (80)	21 (91)	0.393
Other + platinum	4 (20)	2 (9)	
Chemotherapy cycle[b]	5.1 ± 1.6	5.5 ± 1.3	0.295

Abbreviations: CA125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics.
[a] Values are given as mean ± SD or number (percentage), unless indicated otherwise.
[b] 43 patients who received adjuvant chemotherapy were included.

Table 2
Surgical procedures.[a]

Procedure	Fertility-sparing surgery (n = 22)	Radical surgery (n = 25)	*P* value
Total hysterectomy	0	25 (100)	NA
Bilateral salpingo-oophorectomy	0	25 (100)	NA
Unilateral salpingo-oophorectomy	15 (68)	0	NA
Unilateral salpingo-oophorectomy and unilateral ovarian cystectomy	7 (32)	0	NA
Pelvic lymphadenectomy and para-aortic lymphadenectomy	19 (86)	23 (92)	0.654
Omentectomy	20 (91)	23 (92)	>0.99
Appendectomy	13 (59)	19 (76)	0.215

Abbreviation: NA, not applicable.
[a] Values are given as number (percentage), unless indicated otherwise.

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