International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Yoon HS et al. Int J Reprod Contracept Obstet Gynecol. 2023 Jan;12(1):67-71
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20223476

Original Research Article

Survival and reproductive outcome of childbearing age ovarian cancer patients taking fertility-sparing surgery

Hye Soo Yoon[1], Yun Soon Chung[1], Jong Wook Seo[2], Jae Eun Chung[2]*

[1]Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Severance Hospital, Seoul, Republic of Korea
[2]Department of Obstetrics and Gynecology, National Health Insurance Service Ilsan Hospital, Goyang, Republic of Korea

Received: 20 November 2022
Accepted: 10 December 2022

***Correspondence:**
Dr. Jae Eun Chung,
E-mail: jiupark@naver.com

ABSTRACT

Background: Surgical management of ovarian cancer includes total hysterectomy and bilateral salpingo-oophorectomy which results in the loss of fertility. Fertility-sparing surgery in the reproductive aged women with early-stage ovarian cancer with favourable histology has been proposed by American College of Obstetrics and Gynecology and European Society for Medical Oncology. We sought to access the survival and fertility outcome of Korean women in their reproductive age who undertook fertility-sparing surgery.
Methods: Based on the Korean National Insurance Claims Data and the National Health Information Database, 328 women with newly developed ovarian cancer in 2010 were followed up for the survival and pregnancy outcome until 2020. Patients who were diagnosed with cancer or underwent hysterectomy before 2010 were excluded. The control group consisted of 552 women matched by age, economic status and place of living.
Results: Out of 120, 10 deaths occurred in the fertility-sparing surgery group showing a survival rate of 91.7%. Women undertaking fertility-sparing surgery had a lower chance of delivering a new-born compared to the control group (OR 0.46; 95% CI 0.26-0.81). Diagnosis of infertility, ectopic pregnancy, and abortion appeared higher in the fertility-sparing surgery group, but it did not reach a statistical significance.
Conclusions: The pregnancy rate of the ovarian cancer patients with fertility-sparing surgery was lower than that of women without ovarian cancer. Undergoing fertility-sparing surgery per se should not deter women of trying to get pregnant as the pregnancy outcome indicators do not show statistically significant differences compared to the control group.

Keywords: Ovarian cancer, Fertility-sparing surgery, Hysterectomy, Oophorectomy

INTRODUCTION

In 2017, a total of 2,702 women was diagnosed with ovarian cancer and 1,149 died from the disease in Korea.[1] Although the majority of ovarian cancer occur in postmenopausal women reaching a maximum in the seventh decade of life, 3-17% of all epithelial ovarian cancer occur in women of childbearing age.[2] Women in childbearing age with ovarian cancer are more likely to present with early stage disease and lower grade tumors.[3] Standard treatment of ovarian cancer involves total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymph node dissection, followed by adjuvant chemotherapy and second-look surgery in selected cases.[4]

Women who wish to maintain reproductive capability faces the question whether less than radical surgery compromise the patient's survival. Several studies evaluating fertility-sparing surgery in the treatment of ovarian cancer have reported excellent outcome while preserving the patient's reproductive and endocrine

function.[5-10] However, in case of Korean women, only one study involving 62 fertility-sparing cases has been reported so far.[11]

The aim of the study was to evaluate the survival rate and the reproductive outcome of Korean women in their childbearing age treated with fertility-sparing surgery for the ovarian.

METHODS

Based on the Korean National Insurance Claims Database and the National Health Information Database, 328 women from age 15 to 39 with newly developed ovarian cancer in 2010 were followed up for the investigation of the survival and pregnancy outcome until 2020. This study was approved by the National Health Insurance Service Ilsan Hospital institutional review board (NHIS 2021-03-014-001).

Patients with ovarian cancer was defined as having the international classification code 10 (ICD 10) C56.0 with either V193 or V194. The V193 and V194 are special codes assigned by the Korean National Health Insurance Service to Korean patients with cancer, rare diseases, or genetic disorders in order to unburden them economically by curtailing the medical expenses. Of these 328 cases, previous history of cancer diagnosis or treatment, previous hysterectomy status, congenital anomalies affecting fertility, and cases with insufficient data concerning the economic status or place of living were excluded. Ovarian cancer patients who did not take any means of surgeries were excluded as well. The fertility-sparing surgery group was defined as cases involving unilateral oophorectomy without hysterectomy attached with the action codes for the insurance reimbursement such as R4421, R4423, and R4424. Excluding 144 patients who did not meet the inclusion criteria, the resulting 184 patients were allocated in either the conventional operation group who took hysterectomy (n=64) or fertility-sparing surgery group (n=120). Using 1:3 propensity score matching by age, economic status, and place of living, a dataset of control group consisting 552 patients was retrieved. For the investigation of pregnancy outcome, instead of ICD-10 codes for pregnancy diagnosis, action codes of vaginal deliveries and caesarean sections such as R4021 and R4514 were used to ensure actual deliveries of the newborn instead of a mere diagnosis of pregnancy. The diagnosis of infertility, ectopic pregnancy, and abortion was analyzed between the fertility-sparing surgery group and the control group.

All continuous data with normal distribution were expressed as means ± standard deviation. The median and range was utilized for skewed data. Frequency distributions was compared using chi-square test and mean or median values were compared using Student's t and Mann-Whitney U test. Differences between groups were tested using log-rank testing. All calculated p values were two-sided and $p<0.05$ was considered to be statistically significant. Statistical analysis of data was performed using the JMP Statistics package (SAS Institute, Cary, North Carolina, USA).

RESULTS

A total of 328 ovarian cancer cases in women of childbearing age from 15 to 39 were newly diagnosed in 2010. Excluding 144 patients who did not meet the inclusion criteria, out of the 184 patients, 64 cases (34.8%) had conventional operation including hysterectomies and 120 cases (65.2%) undertook fertility-sparing surgery (Figure 1). The characteristics of the ovarian cancer patients and the control including the patient's age, economic status, and place of living are displayed (Table 1).

During the investigation period from 2010 to 2020, 28.1% (18/64) of the conventional surgery group, 8.3% (10/120) of the fertility-sparing group, and 0.7% (4/552) of the control group died. Controlled for the patient's age, economic status, and place of living, HR of death in the conventional operation group was 25.07(HR 25.07; 95% CI 3.94-159.45) and 8.95 in the fertility-sparing group (HR 8.95; 95% CI 1.83-43.63) compared to the control group.

Regarding the pregnancy outcome, 20 out of 120 women in the fertility-sparing operation group had deliveries (16.7%) compared to 143 out of 552 (25.9%) women in the control group. The OR of delivery was lower in the fertility-sparing group (OR 0.46; 95% CI 0.26-0.81). Chances of infertility diagnosis (OR 1.69; 95% CI 0.81-3.54) and acquiring ectopic pregnancy (OR 1.38; 95% CI 0.39-4.86) or abortion (OR 1.62; 95% CI 0.74-3.57) were all higher in the fertility-sparing group but they did not show any statistical significance (Table 2).

Table 1: Patients characteristics summary.

Characteristics	Ovarian cancer patients						Control group N=552		P value 1: (G1+G2) vs control
	G1: Conventional op with hysterectomy (N=64)		G2: Uterus saving op (N=120)		G1+G2 (N=184)				
	N	%	N	%	N	%	N	%	
Age (years)									1.0000
15-24	2	3.1	49	40.8	51	27.7	153	27.7	
25-29	7	10.9	22	18.3	29	15.8	87	15.8	

Continued.

Characteristics	Ovarian cancer patients						Control group N=552		P value 1: (G1+G2) vs control
	G1: Conventional op with hysterectomy (N=64)		G2: Uterus saving op (N=120)		G1+G2 (N=184)				
30-34	13	20.3	29	24.2	42	22.8	126	22.8	
35-39	42	65.6	20	16.7	62	33.7	186	33.7	
Residence									
Seoul	16	25.0	34	28.3	50	27.2	128	23.2	
Suburban	14	21.9	25	20.8	39	21.2	126	22.8	0.5452
Etc.	34	53.1	61	50.8	95	51.6	298	54.0	

Table 2: Odds ratio.

Groups	Infertility			Ectopic pregnancy			Abortion/termination			Live birth		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper
Fertility sparing group	1.69	0.81	3.54	1.38	0.39	4.86	1.62	0.74	3.57	0.46	0.26	0.81
Control	1.00			1.00			1.00			1.00		

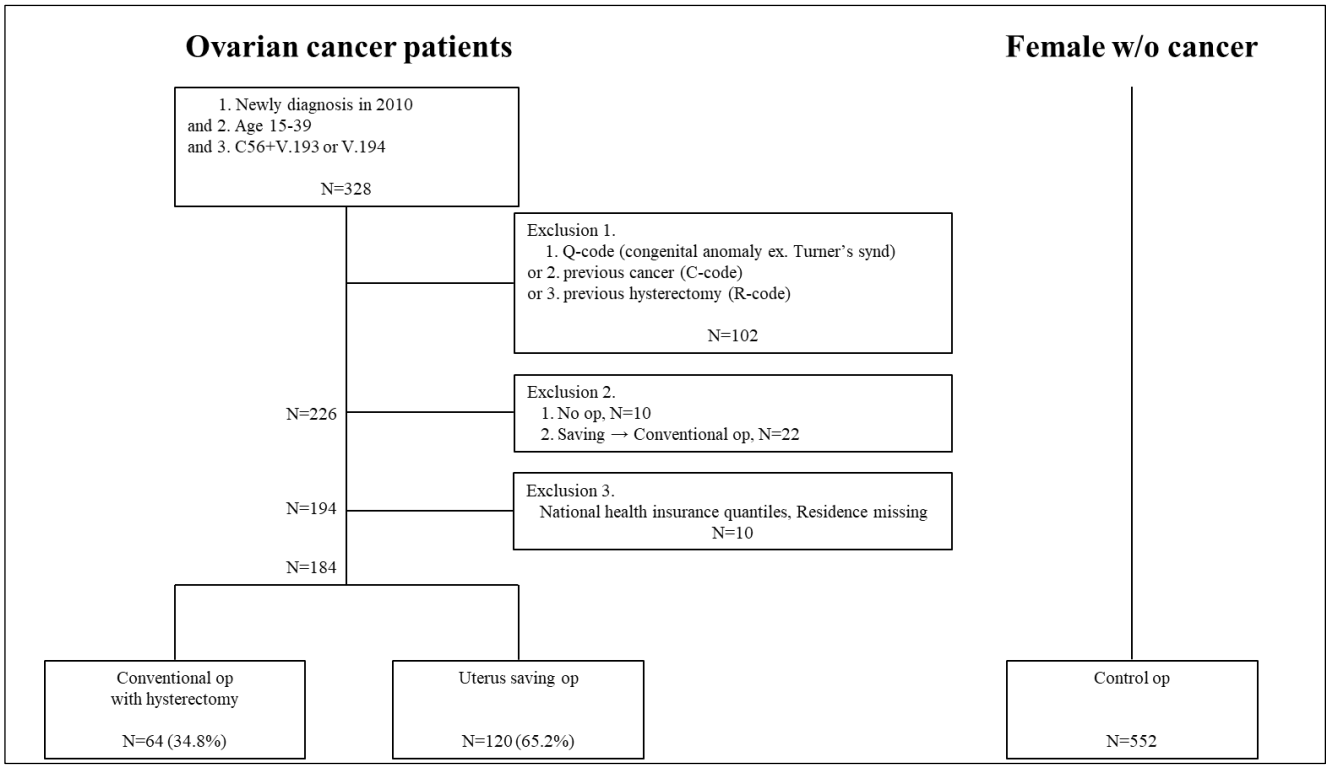

Figure 1: Patient flow chart.

DISCUSSION

The Korean National Insurance Claims Database includes information such as the patient's diagnosis in ICD-10 code, surgeries performed in action codes, years born and deceased of the whole Korean population since 2007. The National Health Information Database provides the patient's age, economic status, and place of living of all the constituents who have undertaken the national health check-up provided by the government free of charge. As the above-mentioned database include the whole Korean population, using these databases gives the study an upper hand in the analysis of disease outcome not confined to a specific medical facility. The authors retrieved data of 328 women with newly developed ovarian cancer in 2010 and analyzed the survival and pregnancy outcome of these women until 2020. Excluding 144 patients who did not meet the inclusion criteria, out of the 184 patients, 64 cases (34.8%) had conventional operation including

hysterectomies and 120 cases (65.2%) undertook fertility-sparing surgery (Figure 1). The control group consisted of 552 women matched by age, economic status and place of living (Table 1).

During the investigation period from 2010 to 2020, 28.1% (18/64) of the conventional surgery group, 8.3% (10/120) of the fertility-sparing group, and 0.7% (4/552) of the control group died. Controlled for the patient's age, economic status, and place of living, HR of death in the conventional operation group was 25.07 (HR 25.07; 95% CI 3.94-159.45) and 8.95 in the fertility-sparing group (HR 8.95; 95% CI 1.83-43.63) compared to the control group. In a series of 52 patients with stage IA and IC ovarian cancer Schilder reported an estimated 5-year survival rate of 98% and concluded that ovarian conservation was safe and was associated with an excellent outcome.[6] Morice and co-workers noted a 5-year survival rate of 82% and concluded that ovarian preservation should be approached cautiously and should be offered only to women with stage IA, grade I tumors.[12] Fertility-sparing surgery for reproductive-age patients with invasive early stage epithelial ovarian cancer has been adopted for stage IA and non-clear cell histology grade 1 and 2 according to the 2007 guidelines of the American College of Obstetrics and Gynecology.[13] The 2008 guidelines of the European Society for Medical Oncology approves fertility-sparing surgery for unilateral stage I tumor without dense adhesions showing favourable histology such as non-clear cell histology.[14] The survival rate of the fertility-sparing group reached 91.7% in our study, but specific indications for the fertility-sparing operation needs to be identified in further studies.

Regarding the pregnancy outcome, 20 out of 120 women in the fertility-sparing group had deliveries (16.7%) compared to 143 out of 552 (25.9%) women in the control group. The OR of delivery was lower in the fertility-sparing group (OR 0.46; 95% CI 0.26-0.81). Chances of infertility diagnosis (OR 1.69; 95% CI 0.81-3.54) and acquiring ectopic pregnancy (OR 1.38; 95% CI 0.39-4.86) or abortion (OR 1.62; 95% CI 0.74-3.57) were all higher in the fertility-sparing group but they did not show any statistical significance (Table 2). Previous investigations have documented successful reproductive function following cancer treatment that is in accord with our result.[15,16]

As this study was not based on the medical record of each patient, histologic findings and specific stage of the cases could not be identified. In weighing the feasibility of fertility-sparing operation, specific tumor types such as malignant ovarian germ cell tumors, sex cord-stromal tumors, tumors of low malignant potential of any stage, and stage IA invasive epithelial cancer should be considered as appropriate candidates.17-20 Some cases might have taken post-operative chemotherapy but data assessing medication was not included in this study. Lastly, as the database does not include medical information that is not covered by the national insurance policy such as infertility treatment, the specifics of the fertility related condition could not be accessed. With proper compensations of these shortcomings, further studies are warranted involving a larger number of patients for a better analysis.

CONCLUSION

Fertility-sparing operation with the right indication in ovarian cancer patients planning for further pregnancy might be considered a safe option. Undergoing fertility-sparing surgery per se should not deter women of trying to get pregnant as the chance of resulting in ectopic pregnancy and abortion showed no statistically significant differences compared to the control group.

Funding: This study has been supported by the National Health Insurance Service Ilsan Hospital (NHIS2021-03-014-001)
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hong S, Won YJ, Park YR, Jung KW, Kong HJ, Lee ES, et al. Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2017. Cancer Res Treat. 2020;52(2):335-50.
2. Rodriguez M, Nguyen HN, Averette HE, Steren AJ, Penalver MA, Harrison T, et al. National survey of ovarian carcinoma XII. Epithelial ovarian malignancies in women less than or equal to 25 years of age. Cancer. 1994;73(4):1245-50.
3. Duska LR, Chang YC, Flynn CE, Chen AH, Goodman A, Fuller AF, et al. Epithelial ovarian carcinoma in the reproductive age group. Cancer. 1999;85(12):2623-9.
4. National Cancer Institute. Cancer Stat Facts: Ovarian cancer, 2021. Available at: https://seer. Cancer.gov/staff acts/html/ovary.html. Accessed on 12 December 2022.
5. Schlaerth AC, Chi DS, Poynor EA, Barakat RR, Brown CL. Long-term survival after fertility-sparing surgery for epithelial ovarian cancer. Int J Gynecol Cancer. 2009;19(7):1199-204.
6. Schilder JM, Thompson AM, DePriest PD, Ueland FR, Cibull ML, Kryscio RJ, et al. Outcome of reproductive age women with stage IA or IC invasive epithelial ovarian cancer treated with fertility-sparing therapy. Gynecol Oncol. 2020;87(1):1-7.
7. Fader AN, Rose PG. Role of surgery in ovarian carcinoma. J Clin Oncol. 2007;25(20):2873-83.
8. Wright JD, Shah M, Mathew L, Burke WM, Culhane J, Goldman N, et al. Fertility preservation in young women with epithelial ovarian cancer. Cancer. 2009;115(18):4118-26.
9. Satoh T, Hatae M, Watanabe Y, Yaegashi N, Ishiko O, Kodama S, et al. Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a

proposal for patient selection. J Clin Oncol. 2010;28(10):1727-32.
10. Gershenson DM. Treatment of ovarian cancer in young women. Clin Obstet Gynecol. 2012;55(1):65-74.
11. Park JY, Kim DY, Suh DS, Kim JH, Kim YM, Kim YT, et al. Outcomes of fertility-sparing surgery for invasive epithelial ovarian cancer: oncologic safety and reproductive outcomes. Gynecol Oncol. 2008;110(3):345-53.
12. Morice P, Wicart-Poque F, Rey A, El-Hassan J, Pautier P, Lhommé C, et al. Results of conservative treatment in epithelial ovarian carcinoma. Cancer. 2001;92(9):2412-8.
13. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin. Management of adnexal masses. Obstet Gynecol. 2007;110(1):201-14.
14. Aebi S, Castiglione M, ESMO Guidelines Working Group. Epithelial ovarian carcinoma: ESMO clinical recommendations for diagnosis, treatment and follow-up. Ann Oncol. 2008;19(2):14-6.
15. Gershenson DM. Menstrual and reproductive function after treatment with combination chemotherapy for malignant ovarian germ cell tumors. J Clin Oncol. 1988;6(2):270-5.
16. Kanazawa K, Suzuki T, Sakumoto K. Treatment of malignant ovarian germ cell tumors with preservation of fertility: reproductive performance after persistent remission. Am J Clin Oncol. 2000;23(3):244-8.
17. Gershenson DM. Management of ovarian germ cell tumors. J Clin Oncol. 2011;61:212-36.
18. Gershenson DM, Hartmann LC, Young RH. Ovarian sex cord-stromal tumors. In: Barakat RR, Markman M, Randall ME, eds. Principles and Practice of Gynecologic Oncology. Philadelphia: Lippincott Williams and Wilkins; 2009: 855-873.
19. Gershenson DM. Fertility-sparing surgery for malignancies in women. J Natl Cancer Inst Monogr. 2005;(34):43-7.
20. Fleming GF, Ronnett BM, Seidman J. Epithelial ovarian cancer. In: Barakat RR, Markman M, Randall ME, eds. Principles and Practice of Gynecologic Oncology. Philadelphia: Lippincott Williams and Wilkins; 2009: 763-835.

Cite this article as: Yoon HS, Chung YS, Seo JW, Chung JE. Survival and reproductive outcome of childbearing age ovarian cancer patients taking fertility-sparing surgery. Int J Reprod Contracept Obstet Gynecol 2023;12:67-71.