PJSS Vol. 66, No. 3, July-September, 2011

PJSS PHILIPPINE JOURNAL OF SURGICAL SPECIALTIES

Outcomes of Patients Undergoing Fertility-Sparing Surgery for Ovarian Cancers: 5-Year Review in a Tertiary Hospital

Ana Victoria V. Dy Echo, M.D., F.P.O.G.S. and Jericho Thaddeus P. Luna, M.D., F.P.O.G.S.

Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines Manila

As ovarian cancer is increasingly diagnosed among reproductive-aged women, fertility sparing surgery (FSS) becomes an important management option.

Objective: A five-year (2005-2009) retrospective study was conducted at a tertiary hospital to determine the fertility and clinical outcomes of ovarian cancer patients who underwent FSS.

Methodology: Patients 16-40 years old who underwent FSS were evaluated. Review of medical records was done to determine clinico-surgico-pathologic demographics. Menstrual, fertility and clinical outcomes were the main outcomes measured.

Results: Forty-four cases (mean age 24 years) were evaluated: 27 epithelial tumors, 16 germ cell tumors and 1 sex cord stromal tumor. Forty-one cases (93.18%) were stage I, while 3 cases (6.82%) had advanced stages. Complete surgical staging was done in 19 (43.18%) patients. At the end of treatment, all patients had restoration of menses 1-2 months after initial surgery with no significant interruption in menses among the 7 patients given platinum-based chemotherapy. There were 15 pregnancies (83.33%), with 2 patients having 2 pregnancies each. There were only 5 patients (27.78%) with infertility, 3 of which already had infertility prior to the surgery. There were 8 (18.18%) cases of tumor persistence/recurrence, all of which were malignant germ cell tumors without adjuvant chemotherapy.

Conclusion: This study suggests that FSS is a safe and acceptable treatment for reproductive-age women, particular those less than 30 years old with no history of infertility, with either stage I epithelial tumors (low malignant potential and frank carcinoma) or malignant germ cell tumors with assured adjuvant chemotherapy.

Key words: fertility-sparing surgery, ovarian cancer

Although ovarian cancer is considered a disease primarily of the postmenopausal women, as much as 20% occur in the reproductive-age group (aged 16-40 years).[1] As young age is associated with increased frequency of early stage, lower grade and low malignant potential disease, survival rates as high as 75% have been reported.[1] With the additional advancement in cancer therapy, more of these women survive long after therapy. As a result, management concern goes beyond provision of a disease-free state to include achieving optimal fertility preserving capacity. Fertility-sparing surgery (FSS) has been proposed as an acceptable management option for these women as long as treatment outcomes are not compromised. The procedure consists of unilateral salpingo-oophorectomy, with preservation of normal-looking uterus and contralateral ovary.

Through the years, the rate of FSS has increased steadily, with reported incidences ranging from 38.1% to 75%.[1,2] The histologic type and extent of the disease are major factors determining feasibility of this treatment modality.[3] The patient's obstetrical history, family medical history, desire to preserve fertility potential and history of infertility are other factors influencing decision to proceed with FSS.[3]

Malignant germ cell tumors,[4,5] malignant sex cord stromal tumors[6] and epithelial tumors of low malignant potential,[4] common among the reproductive-age women, frequently presenting at a very early stage, are associated with excellent overall prognosis and are thus good candidates for FSS.[3,7]

Frank epithelial ovarian carcinomas, on the other hand, are rare among young women, with only 7%-8% stage I tumors diagnosed under 35 years old.[4] At present, there are different recommendations with regards appropriateness of FSS for this histologic type.

The American College of Obstetrics and Gynecology (ACOG) recommends that FSS may be done only for stage IA tumors with grade 1-2 non-clear cell histology.[8] The European Society for Medical Oncology (ESMO) recommends it for any unilateral stage I tumor with a grade 1-2 non-clear cell histology in the absence of dense adhesions.[8] Japanese Society of Gynecologic Oncology (JSGO) extends the recommendation to include unilateral stage IC based on intraoperative rupture and favorable histology.[8]

The effectiveness and limitation of FSS in the management of ovarian cancer remains unclear. The main concerns regarding this therapeutic approach are the risk of recurrence and success of subsequent pregnancy. Some studies have identified the remaining ovary as the main site for recurrence in majority of patients.[9] However, a retrospective study by Zanetta, et al. showed that recurrence rates were similar (9% vs 12%) between epithelial ovarian carcinoma treated with FSS and those who underwent the standard ovarian surgery (hysterectomy with bilateral salpingo-oophorectomy).[10] He likewise noted no difference in overall survival when he compared FSS with the standard surgery in the management of malignant germ cell tumors (overall survival [OS] 90-100% vs. 89-100%).[11] Chan, more recently, also did not see any significant difference (P=0.258) between the 2 surgical approaches, even when he subdivided the epithelial ovarian carcinomas to clear cell and non-clear cell types.[1]

The additional extensive surgical staging procedure that may accompany FSS is commonly associated with postoperative pelvic adhesions. The tendency for postoperative adhesions may be a theoretical disadvantage of FSS as it may be a possible mechanical cause of subsequent infertility. No studies have evaluated a direct correlation between extensive surgical staging and subsequent infertility.

Chemotherapy-induced premature ovarian failure is a particular concern for patients requiring chemotherapy after FSS. Some studies have reported premature menopause by age 31 after chemotherapy in as much as 30%-68% of women.[7] On the other hand, successful pregnancy after chemotherapy has been demonstrated in studies evaluating FSS in malignant germ cell tumors. Zanetta, et al. reported a pregnancy rate of as high as 88% among malignant germ cell tumor patients, regardless of whether subsequent chemotherapy was given or not.[11] Brewer, et al. noted that among women with ovarian dysgerminomas treated with FSS and subsequent chemotherapy, 93% (13/14) resumed normal menstrual cycles after chemotherapy and 5 out of the 14 (36%) had subsequent successful pregnancies.[12] Rouge, et al. reported a pregnancy rate of 75% among women with endodermal sinus tumors who underwent FSS and subsequent chemotherapy.[5] For epithelial ovarian carcinomas, previous regimens involving alkylating agents have been known for its toxic effect on the ovaries, with more than 80% of women developing amenorrhea and subsequent infertility after treatment.[13] On the other hand, the fertility risks of the more recent platinum-based regimen is still unknown.[13]

In the Philippines, the Society of Gynecologic Oncology of the Philippines, Inc. (SGOP) recommends FSS for young patients desirous of pregnancy with stage IA epithelial ovarian carcinoma (low malignant potential and frank carcinoma), stage IA malignant sex cord stromal tumors, all stages of malignant germ cell tumors.[14] However, with all the uncertainties with regards usefulness of FSS, the recommended indications for this procedure remain controversial. This retrospective study aimed to determine Philippine experience with FSS for all types of ovarian cancers.

Objectives

General Objective

To determine the fertility and clinical outcomes of ovarian cancer patients who underwent fertility-sparing surgery (FSS).

Specific Objectives

1. To determine the clinical profile of ovarian cancer patients who underwent FSS
2. To determine the surgico-pathologic factors of ovarian cancer patients who underwent FSS
3. To determine the menstrual and fertility outcome of ovarian cancer patients who underwent FSS

4. To determine the effect of platinum-based chemotherapy on menstrual and fertility outcome of ovarian cancer patients
5. To determine pregnancy outcomes of women who become pregnant after FSS
6. To determine the clinical outcomes of patients who underwent FSS

Methods

Patients diagnosed with ovarian cancer who underwent fertility-sparing surgery (FSS) seen at the Cancer Institute in a tertiary hospital from 2005-2009 were included in this study. FSS included unilateral salpingo-oophorectomy (USO) with preservation of grossly normal-looking uterus and contralateral ovary. The following procedures may or may not have been performed with the USO: contralateral cystectomy, peritoneal fluid cytology (PFC), bilateral pelvic lymph node dissection (BLND), para-aortic lymph node sampling (PALS), infracolic omentectomy (IO), random peritoneal biopsy (RPB) and/or appendectomy. Complete surgical staging was defined as USO, PFC, BLND, PALS, IO, RPB, with or without contralateral cystectomy and appendectomy.

Included in the study were women 16-40 years of age at the time of FSS, diagnosed with any histologic type of ovarian cancer, and any International Federation of Gynecology and Obstetrics (FIGO) stage of ovarian cancer at the time of FSS.

Patients who were receiving therapy for synchronous malignancies, had medical conditions which may interfere with fertility potential, were receiving pelvic radiotherapy, were immunocompromised, or lost to follow-up were excluded from this study.

The study entailed a retrospective review of the Outpatient Medical Records of ovarian cancer patients who underwent FSS seen at the Cancer Institute in a tertiary hospital from 2005-2009. The patients' demographic data (age, parity, obstetric history, history of infertility and family history of breast-ovarian cancer), FIGO stage, histologic type, adjuvant therapy, menstrual pattern and pregnancy outcomes post-FSS, and disease status were recorded in an MS excel database program. Tumors were classified and staged according to the World Health Organization (WHO) Pathologic Classification and 1987 FIGO Staging Classification, respectively. For patients who received adjuvant therapy, the chemotherapeutic regimen, number of cycles and toxicities were recorded.

This study was exempt from IRB review.

Patients with incomplete data but with available contact numbers were contacted by telephone to provide data regarding menstruation patterns and reproductive outcomes after FSS.

The main outcomes measured were as follows: menstrual pattern, fertility outcome and number of pregnancies.

Secondary outcome measured was incidence of tumor persistence or recurrence after FSS. Tumor persistence was defined as presence of detectable tumor, either by physical examination and/or imaging studies with or without CA 125 elevation, at the completion of therapy. Tumor recurrence was defined as development of new tumor, detected by physical examination and/or imaging studies with or without CA 125 elevation, after a complete response to treatment was initially achieved.

The information regarding fertility and clinical outcomes were obtained from entries made during the follow-up of the patients. Otherwise, they were obtained from telephone interview of the patients by the investigator.

The patients' demographic data (age, parity, obstetric history, history of infertility and family history of breast-ovarian cancer), FIGO stage, histologic type, adjuvant therapy, menstrual pattern and pregnancy outcomes post-FSS, and disease status were analyzed using descriptive statistics (mean, range and percentage).

Results

Patient Characteristics

There were a total of 822 ovarian cancer cases seen at the Cancer Institute of the tertiary hospital from 2005-2009. Of these, 116 patients (14%) underwent fertility-sparing surgery (FSS) but 38 medical records were not retrieved and 34 had incomplete data.

A total of 44 patients with a mean age of 24 years ± 5.9 SD (range, 16-38 years) were included in the analysis (Table 1). Thirty patients (68.18%) were nulliparous, with 3 (10%) reporting a history of infertility, at the time of FSS. Fourteen (31.82%) had previous successful pregnancies at the time of surgery. Three (6.82%) had a family history of breast-ovarian cancer.

Table 1. Patient characteristics.

Patient Characteristics (N = 44)		
Characteristic	No.	%
Age, years		
Mean	24	
Range	16-38	
Standard deviation	5.995	
Parity		
Nulliparous	30	68.18
Parous	14	31.82
Family history of breast-ovarian carcinoma	3	6.82
FIGO stage		
IA	34	77.27
IC	7	15.91
III	2	4.55
IV	1	2.27
Histologic type		
Mucinous tumor of low malignant potential	15	34.09
Serous tumor of low malignant potential	2	4.55
Mucinous carcinoma	8	18.18
Endometrioid carcinoma	2	4.55
Dysgerminoma	6	13.64
Immature teratoma	6	13.64
Endodermal sinus tumor	4	9.09
Granulosa cell tumor	1	2.27

There were 27 cases (61.36%) of epithelial ovarian carcinoma: 15 mucinous tumors of low malignant potential, 2 serous tumors of low malignant potential, 8 mucinous carcinomas and 2 endometrioid carcinomas. There were 16 cases (36.36%) of malignant germ cell tumors: 6 dysgerminoma, 6 immature teratoma and 4 endodermal sinus tumor. There was only 1 case (2.27%) of malignant sex cord stromal tumor (granulosa cell tumor).

Majority of the patients (41 cases ~ 93.18%) had stage I disease, 34 stage IA and 7 stage IC. There were only 3 cases (6.82%) with advanced stages, and these were all of germ cell histology.

Surgical Treatments

All of the patients underwent unilateral salpingo-oophorectomy (USO) (Table 2). Of these, 19 (43.18%) had complete surgical staging at the initial surgery, while 25 (56.82%) had incomplete surgical staging procedure. No additional staging surgery was done subsequently on the incompletely-staged patients.

Table 2. Types of surgery in the initial surgery.

Surgery Type	No. of Patients	%
Unilateral salpingo-oophorectomy		
Alone	12	27.27
Incomplete staging	13	29.55
Complete staging (IO, BLND, PALS, RPB)	19	43.18

Adjuvant Chemotherapy

For epithelial ovarian carcinoma (n = 27), there were 4 cases wherein platinum-based adjuvant chemotherapy was recommended: 1 case of stage IA mucinous carcinoma with aneuploidy and 3 cases of stage IC epithelial ovarian carcinomas (1 mucinous tumor of low malignant potential, 1 mucinous carcinoma and 1 endometrioid carcinoma). Only 2 patients (7.41%) completed 6 cycles of chemotherapy. All of the 4 patients had no evidence of disease at the time of evaluation. (Table 3)

For the malignant germ cell tumors (n = 16), platinum-based adjuvant chemotherapy was recommended to patients in the following conditions: immature teratoma with a grade 2 stage IA or where complete surgical

Table 3. Characteristics of patients requiring adjuvant chemotherapy.

Age	Histologic Type	Stage	Platinum-based chemotherapy	Return to menstruation	Fertility outcome	Disease status
21	Mucinous, LMP	IC	Carbo-Pacli VI`	1 month post-chemo	(+) pregnancy	NED
22	Mucinous	IA	Carboplatin VI	1 month post-surgery	(+) pregnancy	NED
24	Mucinous	IC	none	2 months post-surgery	no attempt	NED
36	Endometrioid	IC	none	1 month post-surgery	Infertility*	NED
18	Dysgerminoma	IA	BEP II, EP IV	1 month post-chemo	no attempt	NED
18	Dysgerminoma	IA	none	1 month post-surgery	no attempt	recurrence
16	Endodermal sinus tumor	IC	BEP V	1 month post-surgery	no attempt	NED
17	Endodermal sinus tumor	IC	BEP VI	1 month post-surgery	no attempt	NED
20	Endodermal sinus tumor	IC	BEP III	1 month post-surgery	no attempt	NED
19	Endodermal sinus tumor	IIIB	none	No data	No data	persistence
20	Immature teratoma	IA	none	1 month post-surgery	no attempt	recurrence
17	Immature teratoma	IA	none	1 month post-surgery	no attempt	recurrence
28	Immature teratoma	IA	none	1 month post-surgery	no attempt	recurrence
18	Immature teratoma	IIIC	none	1 month post-surgery	no attempt	recurrence
20	Immature teratoma	IV	BEP II	1 month post-chemo	(+) pregnancy	NED
32	Granulosa cell tumor	IC	none	1 month post-surgery	(+) pregnancy	NED

staging was not performed. Of the 11 patients requiring adjuvant chemotherapy, 5 patients (45.45%) received 2-6 cycles of Bleomycin-Etoposide-Platinum (BEP), with no evidence of disease at the time of evaluation. The 6 patients (54.54%) who did not receive chemotherapy had tumor persistence/recurrence and succumbed to the disease.

The sole case of malignant sex cord stromal tumor was stage IC wherein platinum-based adjuvant chemotherapy was recommended. This patient did not receive any chemotherapy but had no evidence of disease at the end of the study.

Reproductive Outcomes

All patients reported a return of their regular menstrual pattern 1-2 months after FSS. Among the 7 (15.91%) patients who received platinum-based chemotherapy, 3 patients (6.82%) reported a temporary cessation of menses during chemotherapy, with subsequent resumption 1 month post-treatment. The other 4 patients reported having regular menses even during the course of chemotherapy. (Table 3)

Twenty-six of the patients (59.1%) reported having no attempts at pregnancy at the time of evaluation. The remaining 18 patients (40.9%) reported having attempts at pregnancy after FSS. Among those who attempted pregnancy after FSS, 5 (27.78%) reported having infertility, 3 of whom already had histories of infertility prior to FSS. (Table 4)

Isolating patients who underwent complete surgical staging (n = 19), there were 15 patients (78.95%) patients who reported having no attempts at pregnancy at the time of evaluation. Only 4 patients (21.05%) had attempts at pregnancy after FSS. Two had successful pregnancies, while the remaining 2 had problems of infertility, which was present even prior to FSS.

There were a total of 15 (83.33%) reported pregnancies after FSS, with 2 patients having 2 pregnancies each (Table 4). Nine of these pregnancies were full term pregnancies. In the 6 other pregnancies, outcomes were not determined as these patients were eventually lost to follow-up. Among patients who received adjuvant platinum-based chemotherapy (n = 7), 3 attempted and subsequently had successful pregnancies.

Clinical Outcomes

There was only 1 case (2.27%) of tumor persistence after FSS, a case of stage IIIB endodermal sinus

Table 4. Characteristics of patients with attempting pregnancy.

Age	Histologic type	Stage	Surgical Staging	Platinum-based Chemotherapy	Infertility	No. of Pregnancy
37	Mucinous, LMP	IA	Complete	None	Yes	0
33	Mucinous, LMP	IA	Incomplete	None	Yes*	0
25	Mucinous, LMP	IA	Complete	None	Yes	0
38	Serous, LMP	IA	Incomplete	None	Yes*	0
36	Endometrioid	IC	Incomplete	None	Yes*	0
21	Mucinous, LMP	IA	Incomplete	None	None	1
20	Mucinous, LMP	IA	Complete	None	None	1
33	Mucinous, LMP	IA	Incomplete	None	None	2
25	Mucinous, LMP	IA	Incomplete	None	None	2
27	Mucinous, LMP	IA	Incomplete	None	None	1
21	Mucinous, LMP	IC	Incomplete	Carbo-Pacli VI	None	1
26	Serous, LMP	IA	Complete	None	None	1
23	Mucinous	IA	Incomplete	None	None	1
22	Mucinous	IA	Incomplete	Carboplatin VI	None	1
24	Endometrioid	IA	Incomplete	None	None	1
32	Granulosa cell tumor	IC	Incomplete	None	None	1
26	Immature teratoma	IA	Incomplete	None	None	1
20	Immature teratoma	IV	Incomplete	BEP II	None	1

*Patients already reported of infertility prior to initial surgery.

tumor which was incompletely debulked during the initial surgery and the patient did not receive adjuvant chemotherapy. The patient eventually succumbed to the disease.

There were 8 cases (18.18%) of tumor recurrence, all of which were cases of malignant germ cell tumors: 4 cases of stage IA dysgerminoma, 3 cases of stage IA immature teratoma, and 1 case of stage IIIC immature teratoma. All cases did not receive adjuvant chemotherapy. The mean interval for the development of recurrence was 8 months (range, 2-24 months). The main site of recurrence was the pelvic area. None of these patients received additional salvage therapy and eventually succumbed to death.

Discussion

Preservation of fertility is an important, yet controversial, option in the management of ovarian cancer among reproductive aged women. With increasing number of cases diagnosed among those less than 40 years old coupled with subsequent advancement in the management of such disease, more and more women consider subsequent pregnancy after cancer survival. In the present study, fertility-sparing surgery (FSS) was done in 14.11% of cases of ovarian cancer.

Proper selection of patients is important when considering FSS. Age is an important factor. In the present study, the mean age of patients who had FSS was 24 $\pm$ 5.995 SD (range, 16 to 38 years). Although 13/18 (72.22%) generally did not have any problem with fertility after FSS, 4 out of the 5 patients who reported infertility were 33-38 years old. In terms of clinical outcome, age has also been shown to be an independent prognostic for ovarian cancer, with women less than 30 years having grade 1, early stage cancers and thus improved survival.[1] It can thus be suggested that women less than 30 years old will benefit most from FSS, with better reproductive and clinical outcomes compared to those of advanced age.

Patients with a history of infertility may not be good candidates for FSS. In the present study, 3 out of the 5 infertility patients already had such problem even before FSS. As FSS does not provide any fertility advantage for patients with history of infertility, it may provide a possible focus where subsequent recurrence may occur.

The histologic type and stage of ovarian cancer are main factors affecting decision to perform FSS. In the present study, 17 patients (38.64%) had stage I epithelial tumors of low malignant potential, with only 1 patient requiring adjuvant chemotherapy (stage IC). Among these women, 7/11 (63.64%) reported having successful pregnancies, 2 of whom had 2 successive pregnancies. None of the patients developed recurrence at the end of evaluation. This study confirms excellent results of FSS in epithelial tumors of low malignant potential. When diagnosed at an early stage, recurrence rate is only 2.1%.[4] Surgical staging for low malignant potential tumors of the ovary may not be necessary, as survival outcomes of staged and unstaged patients are reported to be the same.[15,16]

There were 10 (22.73%) stage I epithelial ovarian carcinomas who underwent FSS. There were 3/4 successful pregnancies and all had no evidence of disease at the end of evaluation. The Society of Gynecologic Oncology of the Philippines, Inc. (SGOP) recommends FSS as a feasible option only for stage IA and IB, grade 1-2 epithelial ovarian carcinoma, as long as complete surgical staging was done[14], as recurrence rates for these patients are only 2.2%.[8] The present study confirms fertility-sparing surgery as a safe treatment option for stage IA epithelial ovarian carcinoma, even in the absence of complete surgical staging. For stage IC and grade 3 epithelial ovarian carcinomas, FFS is not routinely recommended, as reported recurrence rates are higher (7.9-12.8%).[8] However, the present study suggests that FSS seems to be an acceptable management option for patients with stage IC epithelial ovarian carcinomas. The 2 cases of stage IC epithelial ovarian carcinomas who underwent FSS had no evidence of disease at the end of analysis, regardless of whether complete surgical staging was done and adjuvant chemotherapy given. This is congruent with the result of the study by Satoh, et al. which recommends consideration of FSS for stage IC non-clear cell epithelial ovarian carcinomas.

The current standard treatment for reproductive age women diagnosed with malignant germ cell tumors is to perform FSS, even for advanced stages.[14] However, based on the results of the present study, caution should be made before deciding to proceed with FSS. One case of tumor persistence and 8 cases of tumor recurrence were reported, all of which were of malignant germ cell histology. Unexpectedly, 7 of these cases were diagnosed to have stage IA tumor, 4 of which had complete surgical staging. Good outcome of patients with malignant germ cell tumor relies largely on the success of subsequent chemotherapy. Before the era of chemotherapy, the 3-year survival rates of patients with malignant germ cell tumors were as low as 13%. Thus, FSS may only be offered to patients who can comply with subsequent chemotherapy.

Standard FSS procedure includes unilateral salpingo-oophorectomy (USO) with preservation of the normal looking uterus and contralateral ovary, complete surgical staging [infracolic omentectomy (IO), bilateral pelvic lymph node dissection (BLND), para-aortic lymph node sampling (PALS), random peritoneal biopsies (RPB) $\pm$ appendectomy], followed by adjuvant chemotherapy in selected cases. Inadequate surgical staging and failure to give adjuvant chemotherapy when indicated have theoretical risks in overall clinical outcome of patients treated with FSS. In the present study, only 43.18% of patients had complete surgical staging. Furthermore, among patients requiring adjuvant chemotherapy, only 46.67% received treatment. However, despite the lack of complete surgical staging and provision of adjuvant chemotherapy, clinical outcomes of patients in study, particularly of the epithelial ovarian carcinoma, were excellent, all with no evidence of disease at the end of treatment.

Chemotherapeutic agents have previously been suggested to cause secondary amenorrhea and affect fertility. Ovarian toxicity occurs through impairment of follicular maturation and/or depletion of primordial follicles, and the probability of amenorrhea and infertility is further affected by the patient's age, type, duration and dose of chemotherapy given.[4] Platinum-based adjuvant chemotherapy is presently the standard of treatment for ovarian cancers. Based on different studies, the effect of platinum-based chemotherapy on menstruation and fertility has not been established.[10,11] The present study suggests the safety of platinum-based chemotherapy with regards menstrual and reproductive outcome. Seven patients received platinum-based chemotherapy. Of these, 4 (57.14%) had regular menses during chemotherapy and

the rest eventually had normalization of the menstrual cycle after chemotherapy. The 3 patients who attempted pregnancy successfully became pregnant 8-13 months after completion of therapy (mean duration 9 months). This is in contrast to the study by Satoh, et al. wherein 5% of epithelial ovarian cancer patients treated with platinum-based chemotherapy subsequently developed secondary amenorrhea and infertility.[8] Unlike alkylating agents, platinum-based chemotherapeutic drugs seem to have less toxic effects on ovarian follicles.

Conclusion

Fertility-sparing surgery (FSS) is an acceptable treatment option for reproductive age women diagnosed with ovarian cancer. In particular, it may be an acceptable option for women with the following clinico-surgico-pathologic features: 1) women less than 30 years old with no history of infertility, 2) stage I epithelial tumors (including those with low malignant potential tumor and frank carcinomas), and 3) malignant germ cell tumors, provided adjuvant chemotherapy can be given. Normal menstrual pattern and good fertility outcome are possible after FSS, with or without adjuvant chemotherapy.

Limitations and Recommendations

The retrospective nature of this study contributes a number of limitations to this study. Poor record keeping prevented evaluation of the 116 patients who underwent FSS in the past 5 years. Among the evaluated medical records, most histologic reports failed to specify histologic grading of the tumors, which may be an important prognostic factor that may affect decision for FSS.

One of the objectives of the study was to determine the effect of complete surgical staging to subsequent fertility capacity. Unfortunately, a large percentage of the patients who attempted subsequent pregnancies had incomplete surgical staging. In addition, as most patients who eventually became pregnant did not require or received adjuvant chemotherapy, the effect of chemotherapy to pregnancy outcome could not be evaluated. As a large percentage of women still had no attempts at pregnancy at the time of evaluation, further follow-up of these patients is necessary to completely evaluate the role of complete surgical staging as a possible mechanical factor contributing to infertility.

Estimation of progression-free and overall survival using Kaplan-Meier method would have provided a more objective measure of clinical outcome of patients who underwent FSS, but this would require data on outcomes of patients who underwent standard therapy, which is beyond the scope of this study's methodology.

References

1. Chan JK, Urban R, Cheung MK, Osann K, Husain A, et al. Ovarian cancer in younger vs. older women: a population-based analysis. Br J Cancer 2006; 95: 1314-1320.
2. Rodriguez M, Nuyn HN, Averette HE, Steren AJ, Penalver MA, et al. National survey of ovarian carcinoma XII. Epithelial ovarian malignancies in women less than or equal to 25 years of age. Cancer 1994; 71: 524-529.
3. Gershenson DM. Fertility-sparing surgery for malignancies in women. J Natl Cancer Inst Monograph 2005; 34: 43-47.
4. Simon B, Lee SJ, Partridge AH and Runowicz CD. Preserving fertility after cancer. CA Cancer J Clin 2005; 55: 211-228.
5. Rouge TdM, Pautier P, Duvillard P, Rey A, Morice P, et al. Survival and reproductive function of 52 women treated with surgery and bleomycin, etoposide, cisplatin (BEP) chemotherapy for ovarian yolk sac tumor. Ann Oncol 2008; 19: 1435-1441.
6. Outwater EK, Wagner BJ, Mannion C, McLarney JK and Kim B. Sex cord stromal and steroid cell tumors of the ovary. Radiographics 1998; 18(5): 1523-1546.
7. Leitao MM and Chi DS. Fertility-sparing options for patients with gynecologic malignancies. The Oncologist 2005; 10: 613-622.
8. Satoh T, Hatae M, Watanabe Y, Yaegashi N, Ishiko O, et al. Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient selection. J Clin Oncol 2010; 28(10): 1727-1732.
9. Morice P, Leblanc E, Rey A, Baron M, Querleu D, et al. Conservative treatment in epithelial ovarian cancer: results of a multicentre study of the GCCLCC (Groupe des Chirurgiens de Centre de Lutte Contre le Cancer) and SFOG (Societe Francaise d' Oncologie Gynecologique). Hum Reprod 2005; 20(5): 1379-1385.
10. Zanetta G, Chiari S, Rota S, Bratina G, Maneo A, et al. Conservative surgery for stage I ovarian carcinoma in women of childbearing age. Br J Obstet Gynecol 1997; 104: 1030-1035.
11. Zanetta G, Bonazzi C, Cantu M, Bini S, Locatelli A, et al. Survival and reproductive function after treatment of malignant germ cell ovarian tumors. J Clin Oncol 2001; 19: 1015-1020.
12. Brewer M, Gershenson DM, Herzog CE, Mitchell MF, Silva EG, et al. Outcome and reproductive function after chemotherapy for ovarian dysgerminoma. J Clin Oncol 1999; 17: 2670-2675.
13. Levine J, Canada A and Stern CJ. Fertility preservation in adolescents and young adults with cancer. J Clin Oncol 2010.

14. Society of Gynecologic Oncologists of the Philippines, Inc 2008 Clinical Practice Guidelines. Manila.
15. Winter WE, Kucera PR, Rodgers W, et al. Surgical staging in patients with ovarian tumors of low malignant potential. Obstet Gynecol 2002; 100: 671-676.
16. Rao GG, Skinner E, Gehrig P, et al. Surgical staging of ovarian low malignant potential tumors. Obstet Gynecol 2004; 104: 261-266.