

Fertility sparing surgery in patients with early stage epithelial ovarian cancer: implication of survival analysis and lymphadenectomy

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See accompanying article by Ditto and colleagues on page 320.

Fertility sparing surgery (FSS) has been optioned in patients with early-stage epithelial ovarian cancer (EOC), if they meet several clinicopathologic criteria. Although a variety of studies have reported the outcomes of patients who have undergone FSS and discussed the appropriateness of candidates for this surgical procedure [1-4], one of the major concerns of FSS is a possible increase in recurrence. Indeed, confining to stage I disease, at least three clinicopathologic categories: the International Federation of Gynecology and Obstetrics (FIGO) I substage, tumor differentiation, and histological type, overlap with one another and present an unexpectedly complex manner. It appears safer for FSS to be selected to young women with a well-differentiated stage IA tumor and no sign of invasion of the capsule or positive peritoneal cytology. Actually, stage I patients with stage IC and/or G3 tumor have a greater risk of recurrence and poorer survival than those with stage IA despite platinum-based adjuvant chemotherapy [5]. Moreover, the conclusion of most of previous studies generally focused, not on survival analysis, but on recurrence rates, and so the recommended criteria for FSS remain controversial from guideline to guideline [6,7].

According to sophisticated results from Satoh et al. [8], 5-year overall and recurrence-free survival of stage IC patients excluding clear-cell type and grade 3 tumors were 96.9% and 92.1%, respectively. According to our retrospective data, comparison between the FSS and radical surgery groups revealed no difference in the overall and recurrence-free survival between them, regardless of the stage I substage [9].

Furthermore, based on the large-scale retrospective analysis by Wright et al. [10], ovarian or uterine preservation had no effect on survival compared to a radical surgery group.

Also in this issue of the *Journal of Gynecologic Oncology*, Ditto et al. [11] reported the role and the outcomes of FSS in early-stage EOC patients who underwent comprehensive surgery. They analyzed a total of 36 (18 FSS, 18 radical surgery) patients had a complete surgical staging including lymphadenectomy. As a result, they found seven patients experienced a recurrence (4 in the FSS group and 3 in the radical surgery group). Recurrence-free survival was comparable between the two groups. In this context, the current findings suggest that, among young patients with early-stage EOC, FSS appears to be safe and does not impair survival although further confirmation analyses are needed.

They raised another critical question about necessity of performing retroperitoneal lymphadenectomy as one of the surgical modalities. In many prior reports regarding FSS in EOC, lymphadenectomy was optional. However, the comprehensive surgical staging is in principle necessary for all patients who wish to receive FSS, since CT has a poor sensitivity for low-volume nodal disease. Actually, according to prior studies, patients with tentative stage pT1a EOC had 10%–20% occult tumor metastasis in retroperitoneal lymph node [12,13]. Although exploration of the lymph nodal status is indispensable surgical procedure for accurate staging diagnosis, it is actually difficult because of several serious issues for young women. Assumable benefits of performing comprehensive retroperitoneal lymphadenectomy are thought to be as follows: (1) accurate staging and diagnosis, (2) possibility of omitting additional chemotherapy as a result, (3) possibility of occult tumor removal, and (4) more precisely predict patients'

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oncologic outcome. In contrast, presumable demerits are as follows: (1) a cosmetic problem due to extension of abdominal wound scar, (2) possibility of tubal infertility due to extensive range of adhesion, (3) lack of sufficient evidence showing that lymphadenectomy *per se* can improve patients' prognosis, and (4) few patients who were up-staged by retroperitoneal lymphadenectomy were identified in earlier reports regarding FSS. Assessment of the validity of lymphadenectomy is the one of the most crucial issues to be resolved from here on.

In summary, the several limitations in a number of previous studies have been associated with any retrospective nature. Reflecting on the rarity of subjects receiving FSS, most of earlier articles lacked sufficient individual subgroup analysis. Essentially, the randomized controlled trial is a solution to this problem; however, it is difficult to perform from an ethical aspect. On this occasion, we have a hypothesis that patient with stage I EOC who has undergone FSS may not show a greatly poorer prognosis than we expected, comparing to those receiving radical surgery. Thus, we hope that the hypothesis will be proven by accumulating considerable numbers of patients treated with FSS through a large-scale, clinical registry system in the near future.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Morice P, Leblanc E, Rey A, Baron M, Querleu D, Blanchot J, 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 (Société Française d'Oncologie Gynécologique). *Hum Reprod* 2005;20:1379-85.
2. 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;110:345-53.
3. 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* 2002;87:1-7.
4. Zanetta G, Chiari S, Rota S, Bratina G, Maneo A, Torri V, et al. Conservative surgery for stage I ovarian carcinoma in women of childbearing age. *Br J Obstet Gynaecol* 1997;104:1030-5.
5. Kajiyama H, Mizuno M, Shibata K, Yamamoto E, Kawai M, Nagasaka T, et al. Recurrence-predicting prognostic factors for patients with early-stage epithelial ovarian cancer undergoing fertility-sparing surgery: a multi-institutional study. *Eur J Obstet Gynecol Reprod Biol* 2014;175:97-102.
6. Aebi S, Castiglione M; ESMO Guidelines Working Group. Epithelial ovarian carcinoma: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2008;19 Suppl 2:ii14-6.
7. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: Ovarian cancer including fallopian tube cancer and primary peritoneal cancer. Version 2.2013. Fort Washington, PA: National Comprehensive Cancer Network; 2013.
8. 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;28:1727-32.
9. Kajiyama H, Shibata K, Mizuno M, Umezumi T, Suzuki S, Nawa A, et al. Long-term survival of young women receiving fertility-sparing surgery for ovarian cancer in comparison with those undergoing radical surgery. *Br J Cancer* 2011;105:1288-94.
10. 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;115:4118-26.
11. Ditto A, Martinelli F, Lorusso D, Haeusler E, Carcangiu M, Raspagliesi F. Fertility sparing surgery in early stage epithelial ovarian cancer. *J Gynecol Oncol* 2014;25:320-7.
12. Harter P, Gnauert K, Hils R, Lehmann TG, Fisseler-Eckhoff A, Traut A, et al. Pattern and clinical predictors of lymph node metastases in epithelial ovarian cancer. *Int J Gynecol Cancer* 2007;17:1238-44.
13. Suzuki M, Ohwada M, Yamada T, Kohno T, Sekiguchi I, Sato I. Lymph node metastasis in stage I epithelial ovarian cancer. *Gynecol Oncol* 2000;79:305-8.

