Expert Opinion

J Gynecol Oncol Vol. 26, No. 2:83-86
http://dx.doi.org/10.3802/jgo.2015.26.2.83
pISSN 2005-0380 · eISSN 2005-0399

Journal of Gynecologic Oncology
jgo

Ovarian cancer risk reduction through opportunistic salpingectomy

Janice S. Kwon
Division of Gynecologic Oncology, University of British Columbia and British Columbia Cancer Agency, Vancouver, BC, Canada

There has been increasing evidence over the past decade that the majority of ovarian cancers arise in the fallopian tube and not primarily in the ovary [1-3]. In 2010 the British Columbia Ovarian Cancer Research Group (OVCARE) launched an educational campaign about the potential benefit of "opportunistic salpingectomy" done concurrently with hysterectomy for benign gynecologic conditions, or instead of tubal ligation as surgical sterilization. It was estimated that this practice could reduce ovarian cancer risk by 20% to 40% over the next 20 years [4]. Salpingectomy is favorable to salpingo-oophorectomy because it avoids health risks associated with premature menopause after oophorectomy, including osteoporosis and coronary heart disease [5]. However, there has been skepticism about the safety and absolute benefit of this practice [6,7]. There are no long-term studies confirming that salpingectomy does not compromise ovarian function. Similarly, there are no long-term clinical studies confirming that the fallopian tube is the site of origin of most ovarian cancers. However, the available evidence so far suggests that opportunistic salpingectomy is safe, and likely to be effective and cost-effective as an ovarian cancer prevention strategy.

Based on the British Columbia experience over a 4-year period from 2008 to 2011, opportunistic salpingectomy does not appear to be associated with significant perioperative risks [8]. The average additional operating room time required for salpingectomy was 16 minutes when added to hysterectomy, and 10 minutes when done instead of tubal ligation. While these differences are statistically significant, they are arguably not clinically significant. There was no increased risk of blood transfusion, prolonged hospitalization, or rate of hospital readmission associated with salpingectomy. Minig et al. [9] and Morelli et al. [10] also demonstrated that when salpingectomy was added to laparoscopic hysterectomy, there was no difference in operative time, postoperative hemoglobin, hospital stay, or complication rate. To put perioperative risks into perspective, salpingectomy as an isolated procedure for ectopic pregnancies or *in vitro* fertilization (IVF) has a 1.5% to 1.8% risk [11,12] compared to hysterectomy, which has a 14% to 16% risk based on systematic review [13]. When women are being counseled about salpingectomy as an additional procedure with hysterectomy, they are more likely to experience morbidity as a result of the hysterectomy, not from the salpingectomy. If they undergo tubal ligation, they have a 1.7% perioperative complication rate, which is comparable to salpingectomy [14]. However, the subsequent pregnancy rate is 0.8% after tubal ligation, and inadvertent pregnancy after salpingectomy has yet to be reported (apart from rare cornual pregnancies occurring in patients undergoing IVF).

Opportunistic salpingectomy does not appear to affect ovarian function in the short term. Morelli et al. [10] demonstrated no significant difference in pre- and postoperative levels of anti-Mullerian hormone (AMH), follicle stimulating hormone (FSH), antral follicle count, mean ovarian diameter, and peak systolic velocity, as measures of ovarian function assessed 3 months after hysterectomy [10]. Findley et al. [15] also demonstrated no significant difference in baseline and postoperative AMH levels 3 months after laparoscopic hysterectomy. Other authors have reported that bilateral salpingectomy does not affect ovarian reserve or response to gonadotropin stimulation for IVF treatment [16,17]. On the other hand, Ye et al. [18] reported that bilateral salpingectomy was associated in decreased AMH and increased FSH levels in women seeking IVF, compared to those not having tubal surgery. These authors suggested that salpingectomy undermines

Received Apr 1, 2015, **Accepted** Apr 1, 2015

Correspondence to Janice Kwon
Division of Gynecologic Oncology, University of British Columbia and BC Cancer Agency, 2775 Laurel Street, 6th Floor, Vancouver, BC, Canada V5Z 1M9. E-mail: Janice.Kwon@vch.ca

ovarian reserve, although there was no difference in the total number of follicles and oocytes retrieved from both ovaries. However, women having opportunistic salpingectomy are either undergoing hysterectomy or permanent sterilization, and therefore response to gonadotropic stimulation for fertility treatment is arguably not the most relevant outcome measure. Vorwergk et al. [19] also reported no significant differences in duration of surgery, intraoperative complications, and length of hospitalization between those undergoing hysterectomy alone compared to those having hysterectomy with salpingectomy. Yet, there was a significant difference in the proportion having adnexal pathology during follow-up (26.9% vs. 13.9%, p=0.02, for hysterectomy without and with salpingectomy, respectively) [19]. Other authors have reported increased risks after hysterectomy alone, including immediate postoperative infection [20], hydrosalpinx [21], tubo-ovarian abscess and pyosalpinx, and tubal prolapse, torsion, and pregnancy [22]. It is also important to recognize that ovarian failure is accelerated after hysterectomy, even without salpingectomy. Menopause occurs in 20% of women within 5 years of hysterectomy, or about 4 years earlier than without hysterectomy [23,24]. One of the theories is that hysterectomy affects blood flow to the ovaries, which could compromise their function [25].

Kwon et al. [26] reported that opportunistic salpingectomy should be effective in reducing the number of future ovarian cancer cases at acceptable cost. Salpingectomy with hysterectomy was found to be less costly and more effective than hysterectomy alone, in terms of reducing the number of subsequent ovarian cancer cases and prolonging average life expectancy. Salpingectomy is more costly than tubal ligation in terms of operative time and the potential for perioperative complications; however, it is more likely to be effective in reducing ovarian cancer risk. The ICER (incremental cost-effective ratio) for salpingectomy relative to tubal ligation was $27,278 per year of life gained, and therefore it would be considered a cost-effective alternative for surgical sterilization, being below the conventional North American threshold of $50,000 per year of life gained [27]. The absolute benefit from opportunistic salpingectomy is estimated at a number needed to treat (NNT) of 273 to prevent one case of ovarian cancer during hysterectomy, and NNT of 366 for surgical sterilization (instead of tubal ligation). While these NNT estimates seem high, they are comparable to the NNT of 324 to prevent one case of cervical cancer with human papilloma virus vaccination [28], which reflect the relatively low incidence of ovarian and cervical cancers in our population.

If opportunistic salpingectomy reduces the number of ovarian cancer cases compared to hysterectomy alone or tubal ligation, this will in turn reduce future health care costs associated with ovarian cancer treatment [26]. The advantage of the analysis by Kwon et al. [26] is that it estimates the costs and benefits of opportunistic salpingectomy in a large cohort of women requiring hysterectomy for benign conditions, or surgical sterilization, which would be difficult to obtain from a clinical trial or cohort study. There remains uncertainty about the long-term impact on ovarian function and absolute reduction in ovarian cancer risk from salpingectomy. However, there is still no effective screening test for ovarian cancer [29,30], and there are no alternatives for ovarian cancer risk reduction that can be offered with minimal morbidity and cost. The oral contraceptive pill (OCP) reduces ovarian cancer risk by 50% if used for more than 5 years [31], which appears comparable to opportunistic salpingectomy. Yet, OCPs are associated with increased risks of breast and cervical cancer and thromboembolic events, such that the cumulative risk is likely to be equivalent or greater than the decreased risk in ovarian cancer [31], and this precludes the routine use of OCPs for the primary prevention of ovarian cancer.

There may be many more opportunities to expand the use of opportunistic salpingectomy. While this procedure is usually done by open or laparoscopic surgery, the majority of patients with normal-sized mobile adnexae can have these successfully removed at the time of vaginal hysterectomy as well, with reported rates between 66% and 99% [32-36]. Even if the entire fallopian tube cannot be removed at vaginal hysterectomy, it is the distal portion of the tube in which the vast majority (over 90%) of high-grade serous carcinomas appear to arise [1,3], and this should be accessible after the uterus is removed, or possibly with the assistance of vaginal laparoscopy [37]. Finally, gynecologic patients represent only a subgroup of women requiring abdominal or pelvic surgery. Opportunistic salpingectomy could be done at the time of other surgical procedures (e.g., appendectomy, cholecystectomy), thereby extending the risk-reducing potential even further to other women in the general population.

This year the American College of Obstetrics and Gynecology published a Committee Opinion on Salpingectomy for Ovarian Cancer Prevention [38]. This document acknowledges the problems associated with screening for ovarian cancer, and the potential for prophylactic salpingectomy to prevent ovarian cancer. It also advises that the approach to hysterectomy or sterilization should not be influenced by the potential benefit of salpingectomy, and that randomized trials are required to support the validity of this intervention. We agree that prospective evaluation of salpingectomy with hysterectomy or instead of tubal ligation is still essential to determine the long-term impact on ovarian function, ovarian cancer

 http://dx.doi.org/10.3802/jgo.2015.26.2.83

incidence, and mortality; however, these outcomes will remain unknown for at least another one or two decades. Until then, opportunistic salpingectomy (electively with hysterectomy, or instead of tubal ligation) appears to be safe and cost-effective, and should be considered for women requiring these gynecologic procedures.

CONFLICT OF INTEREST

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

REFERENCES

1. Kindelberger DW, Lee Y, Miron A, Hirsch MS, Feltmate C, Medeiros F, et al. Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: evidence for a causal relationship. Am J Surg Pathol 2007;31:161-9.
2. Piek JM, van Diest PJ, Zweemer RP, Jansen JW, Poort-Keesom RJ, Menko FH, et al. Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. J Pathol 2001;195:451-6.
3. Przybycin CG, Kurman RJ, Ronnett BM, Shih Ie M, Vang R. Are all pelvic (nonuterine) serous carcinomas of tubal origin? Am J Surg Pathol 2010;34:1407-16.
4. BC's Ovarian Cancer Research Team. Advocating Fallopian Tube removal at the time of hysterectomy to prevent ovarian cancer [Internet]. Vancouver, BC: OVCARE; c2013 [cited 2015 Mar 30]. Available from: http://www.ovcare.ca/prevention/for_health_professionals.
5. Parker WH, Feskanich D, Broder MS, Chang E, Shoupe D, Farquhar CM, et al. Long-term mortality associated with oophorectomy compared with ovarian conservation in the nurses' health study. Obstet Gynecol 2013;121:709-16.
6. Herzog TJ, Dinkelspiel HE. Fallopian tube removal: "stic-ing" it to ovarian cancer: what is the utility of prophylactic tubal removal? Curr Oncol 2013;20:148-51.
7. Narod SA. Salpingectomy to prevent ovarian cancer: a counter-currents series. Curr Oncol 2013;20:145-7.
8. McAlpine JN, Hanley GE, Woo MM, Tone AA, Rozenberg N, Swenerton KD, et al. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. Am J Obstet Gynecol 2014;210:471.e1-11.
9. Minig L, Chuang L, Patrono MG, Cardenas-Rebollo JM, Garcia-Donas J. Surgical outcomes and complications of prophylactic salpingectomy at the time of benign hysterectomy in premenopausal women. J Minim Invasive Gynecol 2015 Feb 23 [Epub]. http://dx.doi.org/10.1016/j.jmig.2015.02.013.
10. Morelli M, Venturella R, Mocciaro R, Di Cello A, Rania E, Lico D, et al. Prophylactic salpingectomy in premenopausal low-risk women for ovarian cancer: primum non nocere. Gynecol Oncol 2013;129:448-51.
11. Dubuisson JB, Morice P, Chapron C, De Gayffier A, Mouelhi T. Salpingectomy: the laparoscopic surgical choice for ectopic pregnancy. Hum Reprod 1996;11:1199-203.
12. Strandell A, Lindhard A, Waldenstrom U, Thorburn J, Janson PO, Hamberger L. Hydrosalpinx and IVF outcome: a prospective, randomized multicentre trial in Scandinavia on salpingectomy prior to IVF. Hum Reprod 1999;14:2762-9.
13. Bijen CB, Vermeulen KM, Mourits MJ, de Bock GH. Costs and effects of abdominal versus laparoscopic hysterectomy: systematic review of controlled trials. PLoS One 2009;4:e7340.
14. Bhiwandiwala PP, Mumford SD, Feldblum PJ. A comparison of different laparoscopic sterilization occlusion techniques in 24,439 procedures. Am J Obstet Gynecol 1982;144:319-31.
15. Findley AD, Siedhoff MT, Hobbs KA, Steege JF, Carey ET, McCall CA, et al. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial. Fertil Steril 2013;100:1704-8.
16. Lin YJ, Ou YC, Huang FJ, Lin PY, Kung FT, Lan KC. Ovarian response to gonadotropins in patients with tubal factor infertility: salpingectomy versus nonsalpingectomy. J Minim Invasive Gynecol 2013;20:637-41.
17. Ni L, Sadiq S, Mao Y, Cui Y, Wang W, Liu J. Influence of various tubal surgeries to serum antimullerian hormone level and outcome of the subsequent IVF-ET treatment. Gynecol Endocrinol 2013;29:345-9.
18. Ye XP, Yang YZ, Sun XX. A retrospective analysis of the effect of salpingectomy on serum antiMullerian hormone level and ovarian reserve. Am J Obstet Gynecol 2015;212:53.e1-10.
19. Vorwergk J, Radosa MP, Nicolaus K, Baus N, Jimenez Cruz J, Rengsberger M, et al. Prophylactic bilateral salpingectomy (PBS) to reduce ovarian cancer risk incorporated in standard premenopausal hysterectomy: complications and re-operation rate. J Cancer Res Clin Oncol 2014;140:859-65.
20. Repasy I, Lendvai V, Koppan A, Bodis J, Koppan M. Effect of the removal of the Fallopian tube during hysterectomy on ovarian survival: the orphan ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2009;144:64-7.
21. Morse AN, Schroeder CB, Magrina JF, Webb MJ, Wollan PC, Yawn BP. The risk of hydrosalpinx formation and adnexectomy following tubal ligation and subsequent hysterectomy: a historical cohort study. Am J Obstet Gynecol 2006;194:1273-6.
22. Ghezzi F, Cromi A, Siesto G, Bergamini V, Zefiro F, Bolis P. Infectious morbidity after total laparoscopic hysterectomy: does concomitant salpingectomy make a difference? BJOG 2009;116:589-93.
23. Moorman PG, Myers ER, Schildkraut JM, Iversen ES, Wang F, Warren N. Effect of hysterectomy with ovarian preservation on ovarian function. Obstet Gynecol 2011;118:1271-9.
24. Farquhar CM, Sadler L, Harvey SA, Stewart AW. The association of hysterectomy and menopause: a prospective cohort study. BJOG 2005;112:956-62.
25. Siddle N, Sarrel P, Whitehead M. The effect of hysterectomy on the age at ovarian failure: identification of a subgroup of women with premature loss of ovarian function and literature review. Fertil Steril 1987;47:94-100.

26. Kwon JS, McAlpine JN, Hanley GE, Finlayson SJ, Cohen T, Miller DM, et al. Costs and benefits of opportunistic salpingectomy as an ovarian cancer prevention strategy. Obstet Gynecol 2015;125:338-45.
27. King JT Jr, Tsevat J, Lave JR, Roberts MS. Willingness to pay for a quality-adjusted life year: implications for societal health care resource allocation. Med Decis Making 2005;25:667-77.
28. Brisson M, Van de Velde N, De Wals P, Boily MC. Estimating the number needed to vaccinate to prevent diseases and death related to human papillomavirus infection. CMAJ 2007;177:464-8.
29. Menon U, Gentry-Maharaj A, Hallett R, Ryan A, Burnell M, Sharma A, et al. Sensitivity and specificity of multimodal and ultrasound screening for ovarian cancer, and stage distribution of detected cancers: results of the prevalence screen of the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). Lancet Oncol 2009;10:327-40.
30. Partridge E, Kreimer AR, Greenlee RT, Williams C, Xu JL, Church TR, et al. Results from four rounds of ovarian cancer screening in a randomized trial. Obstet Gynecol 2009;113:775-82.
31. Havrilesky LJ, Moorman PG, Lowery WJ, Gierisch JM, Coeytaux RR, Urrutia RP, et al. Oral contraceptive pills as primary prevention for ovarian cancer: a systematic review and meta-analysis. Obstet Gynecol 2013;122:139-47.
32. Camanni M, Mistrangelo E, Febo G, Ferrero B, Deltetto F. Prophylactic bilateral oophorectomy during vaginal hysterectomy for benign pathology. Arch Gynecol Obstet 2009;280:87-90.
33. Candiani M, Izzo S, Bulfoni A, Riparini J, Ronzoni S, Marconi A. Laparoscopic vs vaginal hysterectomy for benign pathology. Am J Obstet Gynecol 2009;200:368.e1-7.
34. Cho HY, Kang SW, Kim HB, Park SH, Park ST. Prophylactic adnexectomy along with vaginal hysterectomy for benign pathology. Arch Gynecol Obstet 2012;286:1221-5.
35. Karp DR, Mukati M, Smith AL, Suciu G, Aguilar VC, Davila GW. Predictors of successful salpingo-oophorectomy at the time of vaginal hysterectomy. J Minim Invasive Gynecol 2012;19:58-62.
36. Cruikshank SH, Kovac SR. Randomized comparison of three surgical methods used at the time of vaginal hysterectomy to prevent posterior enterocele. Am J Obstet Gynecol 1999;180:859-65.
37. Shepherd JP, Zyczynski HM. Removal of adnexa at the time of vaginal hysterectomy. Clin Obstet Gynecol 2010;53:17-25.
38. Committee on Gynecologic Practice. Committee opinion no. 620: salpingectomy for ovarian cancer prevention. Obstet Gynecol 2015;125:279-81.

 http://dx.doi.org/10.3802/jgo.2015.26.2.83