

VIEWPOINT

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Salpingectomy in Ovarian Cancer Prevention

Nearly 20 000 women are diagnosed with ovarian cancer in the US each year, and approximately 80% have the most lethal subtype: high-grade serous carcinoma. The vast majority of patients have no risk factors, have widely metastatic disease at symptom onset, and die within 5 years of diagnosis. Hope for efficacious screening and prevention strategies has been long-standing. The recent results of the United Kingdom Collaborative Trial of Ovarian Cancer Screening, the largest ovarian cancer screening trial in history, were unsettling. Although screening resulted in an increase in earlier-stage diagnosis, this did not translate into lives saved.¹

Efforts to develop screening for ovarian cancer have been unsuccessful, in large part because of the uncertainty about the exact origin of the disease. For more than a century, physicians and scientists hypothesized that high-grade serous carcinoma arises from ovarian surface epithelium. However, accumulating epidemiological, clinical, pathological, and molecular data over the past 20 years indicate that high-grade serous carcinoma primarily originates from microscopic precancers in the fimbriated ends of fallopian tubes, rather than from the ovary itself. Unfortunately, the fallopian tube cannot be visualized using clinical-grade imaging, and there is no blood test to detect the early, yet rapidly

Since 2011, many national-level organizations worldwide have endorsed opportunistic salpingectomy as a practical, population-level approach to ovarian cancer prevention. Universal uptake of salpingectomy during hysterectomy and in lieu of tubal ligation could prevent nearly 2000 deaths from ovarian cancer per year and save a half billion health care dollars in the US annually.⁴ Given these potential benefits, opportunistic salpingectomy must become standard of surgical care, and efforts are needed to ensure tubal ligation and hysterectomy without salpingectomy for postreproductive women become obsolete.

How Can Opportunistic Salpingectomy Expand Beyond Gynecologic Surgery to Save More Lives?

Most surgical procedures for cancer prevention compromise form or function (eg, mastectomy, oophorectomy, colectomy) or are undertaken to prevent an exceedingly rare cancer (eg, appendectomy for appendiceal cancer, which affects just 1 per 1 million individuals). The advantage of preventing ovarian cancer, 1 of the top 5 most dangerous cancers in women, by removing the fallopian tube, a structure that has no form or function after childbearing years, is unprecedented in the history of medicine. In their postreproductive years, hundreds of thousands of women undergo abdominal surgery, such as cholecystectomy, hernia repair, appendectomy, and gastrointestinal and urologic operations. These are windows of opportunity for opportunistic salpingectomy beyond gynecologic surgery.

Regretfully, there has been low uptake of opportunistic salpingectomy as a cancer preventive intervention. Accord-

ing to patients, their lack of awareness about opportunistic salpingectomy is the key barrier to implementation in gynecologic surgery.⁵ This is compounded by major knowledge gaps within the medical field. Many health care professionals are not yet aware of the discovery that ovarian cancer arises from the fallopian tubes and need to be apprised of where opportunistic salpingectomy fits into reproductive medicine.

In addition, there is no established approach to integrate a surgical procedure for cancer prevention that spans across surgical specialties. Siloes in surgical training and institutions breed unique specialty-specific subcultures that undermine teamwork to care for patients. In particular, gynecologic surgeons in departments of obstetrics and gynecology are distanced from the larger surgical community, creating unique organizational challenges for adopting a population-based approach to ovarian cancer prevention beyond the obstetrics and gynecology space. Careful process mapping to enrich cross-specialty partnership, as opposed to relocating

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spreading, peritoneal metastasis characteristic of high-grade serous carcinoma.

In 2022, Canadian researchers² published the first prospective evidence that surgical removal of both fallopian tubes (bilateral salpingectomy) may substantially decrease high-grade serous carcinoma risk for women in the general population. At the time of follow-up, no high-grade serous carcinoma was observed among the 25 889 women who had undergone salpingectomy during hysterectomy or in lieu of tubal ligation for sterilization. Gynecologic surgeons use the term *opportunistic salpingectomy* to describe salpingectomy for the primary prevention of ovarian cancer in women who undergo pelvic surgery for another indication (eg, hysterectomy).³ Excision of the postreproductive fallopian tube, which has no crucial form or function, is low risk for patients. However, removal of the ovaries can have adverse health effects because the ovaries are important endocrine organs that likely function beyond menopause.

gynecologic surgeons to surgery departments, would be most strategic. Efforts to expand surgical prevention of ovarian cancer will require unprecedented collaboration and shared commitment among gynecologic and nongynecologic surgeons, as well as the medical community at large.

That opportunistic salpingectomy by definition is *surgical sterilization* presents formidable obstacles from state and federal policy to coding, billing, and insurance reimbursement. Existing Medicaid policies preclude thousands of patients from accessing surgical sterilization,⁶ and medical coding is not current for many procedures that are beneficial to the health of women, transgender men, and nonbinary individuals. For example, there is no explicit third-party coverage for opportunistic salpingectomy and, importantly, there is no basis for reimbursement for opportunistic salpingectomy for menopausal individuals or those with a history of tubal ligation because it cannot be coded and billed as surgical sterilization. Medical coding deficiencies for cancer-preventive surgeries like salpingectomy can lead to insurance denials that, if not addressed from the outset, will hinder patient access and health care clinician engagement.

Another major obstacle to realizing the maximal benefit for opportunistic salpingectomy relates to shortcomings inherent to the current histopathologic assessment of fallopian tubes. Serous tubal intraepithelial carcinoma is stage 0 in situ disease and may be detected at the time of salpingectomy. This finding portends future development of high-grade serous carcinoma of the peritoneum (primary peritoneal cancer); however, the current diagnostic techniques lack sensitivity, have poor reproducibility, and are labor intensive.⁷ Reliably identifying serous tubal intraepithelial carcinoma is a major diagnostic challenge that must be addressed in order to bridge the gap between cancer prevention and interception. The surface area of the fimbriated end of the fallopian tube is considerable, and its precancerous cells are infinitesimally small. Pathologists only examine a small portion of the fallopian tube—some estimate less than 1%—to determine a final histopathologic diagnosis.⁸ Because the majority of tissue remains unexamined,

there is considerable risk of missing precancerous cells. Thus, engineering solutions to improve the throughput and sensitivity of diagnostic techniques is critical to decreasing mortality from the entire spectrum of high-grade serous carcinoma.

Fallopian tube removal for ovarian cancer prevention was publicized in recent media coverage; however, a path forward was not presented.⁹ The medical community's vision and execution of increasing knowledge of and access to ovarian cancer prevention by salpingectomy must be grounded in science, equity, and patient safety. On the clinical side, there must be improved surgeon awareness to facilitate adoption of this life-saving approach. These efforts, in addition to a multisite prospective trial to establish the acceptability and feasibility of salpingectomy at the time of nongynecologic abdominal surgery, should be the foundation for a data-driven approach.

To gauge equitable access, measure efficacy, determine long-term outcomes, and facilitate development of risk-prediction modeling, a national salpingectomy registry that collates histopathologic, molecular, genetic, and clinical data is needed. Provision of salpingectomy to eligible patients (postreproductive individuals with no genetic risk of ovarian cancer undergoing another abdominal or pelvic procedure) should also be recognized as a quality metric and prospectively added to the National Surgical Quality Improvement Program database. Simultaneously, researchers must develop engineering solutions to address current diagnostic limitations that can be easily integrated into clinical practice and that yield clinically actionable scientific discoveries.

Forging the standard of care for salpingectomy in ovarian cancer prevention will be a significant effort that requires radical collaboration between gynecologic and nongynecologic surgeons in ways that transform surgical culture. Knowledge translation must permeate the breadth of medicine and be unified across all sources that patients rely on for advice and referral. Expansion of opportunistic salpingectomy for the surgical prevention of ovarian cancer in the US will save lives, but to do so, adeptly overcoming the evident and unforeseen obstacles is mission critical.

ARTICLE INFORMATION

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REFERENCES

- Menon U, Gentry-Maharaj A, Burnell M, et al. Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. *Lancet*. 2021;397(10290):2182-2193. doi:10.1016/S0140-6736(21)00731-5
- Hanley GE, Pearce CL, Talhouk A, et al. Outcomes from opportunistic salpingectomy for

ovarian cancer prevention. *JAMA Netw Open*. 2022; 5(2):e2147343. doi:10.1001/jamanetworkopen.2021.47343

3. American College of Obstetricians and Gynecologists. ACOG committee opinion No. 744: opportunistic salpingectomy as a strategy for epithelial ovarian cancer prevention. *Obstet Gynecol*. 2019;133(4):842-843. doi:10.1097/AOG.0000000000003165

4. Naumann RW, Hughes BN, Brown J, Drury LK, Herzog TJ. The impact of opportunistic salpingectomy on ovarian cancer mortality and healthcare costs: a call for universal insurance coverage. *Am J Obstet Gynecol*. 2021;225(4):397.e1-397.e6. doi:10.1016/j.ajog.2021.03.032

5. Gelderblom ME, Van Lieshout LAM, Piek MJM, De Hullu JA, Hermens RPMG. Patients' and professionals' perspectives on implementation of opportunistic salpingectomy: a mixed-method study. *BMC Health Serv Res*. 2021;21(1):736. doi:10.1186/s12913-021-06767-9

6. Borrero S, Zite N, Potter JE, Trussell J. Medicaid policy on sterilization—anachronistic or still relevant? *N Engl J Med*. 2014;370(2):102-104. doi:10.1056/NEJMp1313325

7. Steenbeek MP, van Bommel MHD, Bulten J, et al. Risk of peritoneal carcinomatosis after risk-reducing salpingo-oophorectomy: a systematic review and individual patient data meta-analysis. *J Clin Oncol*. 2022;40(17):1879-1891. doi:10.1200/JCO.21.02016

8. Vang R, Wheeler JE. Diseases of the fallopian tube and paratubal region. In: Kurman RJ, Ellenson LH, Ronnett BM, eds. *Blaustein's Pathology of the Female Genital Tract*. Springer; 2011. doi:10.1007/978-1-4419-0489-8_11

9. Rabin RC. To prevent cancer, more women should consider removing fallopian tubes, experts say. *New York Times*; February 1, 2023. Accessed May 23, 2023. <https://www.nytimes.com/2023/02/01/health/ovarian-cancer-fallopian-tubes.html>