

Opportunistic Salpingectomy as an Ovarian Cancer Primary Prevention Strategy

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Abstract Ovarian cancer is the most lethal form of all gynecologic malignancies. The presenting clinical symptoms of ovarian cancer are very vague and often appear late in the course of disease. Hence, most patients are diagnosed at later stages. At present, there is no effective screening of ovarian cancer. Primary prevention could be considered a strategy to decrease the mortality from ovarian cancer, not only in women at high risk but also in those at low risk. Most “ovarian cancers,” and more specifically the high-grade serous carcinoma (HGSC) subtype of

ovarian cancer, actually could originate in the fallopian tube. Women who have known BRCA1 or BRCA2 germline mutations should be counseled regarding bilateral salpingo-oophorectomy, immediately after completion of childbearing, as the best strategy for reducing their risk of developing ovarian cancer. If the patient is reluctant, they should be counseled regarding risk-reducing salpingectomy when childbearing is complete followed by oophorectomy in the future. For women at average risk of ovarian cancer, risk-reducing salpingectomy should also be discussed and considered with patients at the time of any abdominal or pelvic surgery, hysterectomy or tubal ligation.

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The Problem of Ovarian Cancer

Ovarian cancer is the most lethal form of all gynecologic malignancy. India has an estimated 1 million cases of cancer and 700,000 cancer deaths according to a 2012 GLOBOCAN report. In most of the population-based cancer registries in India, from where we get Indian data, ovarian cancer is the third leading cause of cancer among women, next to cervix and breast cancer. Cancer registries have also highlighted that more than 70% of cancers in females occur in the age group of 35–64 and that these cancers exercise an adverse influence on the productive role of women in our society. More than half of ovarian cancers also occur in the reproductive age group, compromising the reproductive potential. The increasing incidence of cancer in India has mirrored trends in developed countries. As the world's population ages, remarkable increase in the total number of ovarian cancer cases is expected. The problem is compounded by the fact that we do not have any organized national cancer screening programs. Further, there is an unequal distribution of care providers in northern and southern states. Lack of access to healthcare services and absence of awareness of ovarian cancer in the population are major hindrances to the presentation and management [1].

The main factor behind the poor survival rates of ovarian cancer is the stage at presentation and diagnosis. One-third of the patients present with stage I disease, and five-year survival rates exceed 90%. Approximately 65% of patients present with widespread (stages III or IV) disease, at which point cure is not possible. Although 50–75% of patients treated with chemotherapy initially respond to the medications, most will have recurrences of the disease [2].

Ovarian Cancer Screening as It Exists Today

The presenting clinical symptoms of ovarian cancer are very vague and often appear late in the course of disease. Hence, most patients are diagnosed at later stages after the disease has disseminated throughout the peritoneal cavity. Also, the symptoms may be non-specific and not taken seriously by the patient and the doctor even if the patient presents with some symptoms. Although many attempts have been made to develop screening programs in India for asymptomatic women aimed at detecting early-stage disease in ovarian cancer, current screening methods have disadvantage of low sensitivity and specificity, high false-positive rates, and an unfavorable balance between the risks of early intervention and the benefits of cancer risk reduction. At present, there is no effective screening of ovarian cancer [3].

Some methods for screening suggested by various groups include annual pelvic examination, annual pelvic ultrasound with ovarian volume, and marker evaluation. Specifically, screened subjects underwent unnecessary surgeries that did not diagnose ovarian cancer eventually and were associated with intraoperative and postoperative complications. Hence, The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial found that screening did more harm than good with respect to ovarian cancer. The UK Collaborative Trial of Ovarian Cancer Screening, 2015, found that serial testing of the cancer antigen 125 protein, interpreted according to the Risk of Ovarian Cancer Algorithm (ROCA), and ultrasound were better at detecting ovarian cancer than a single threshold CA 125 test. So a series of CA125 tests were suggested wherein a rising value was of significance. They concluded that clinicians must maintain a high index of suspicion toward ovarian cancer when they see a patient to clinically diagnose it, instead of resorting to screening [4].

Due to the absence of an effective screening program for assessing risk or clinical symptoms that develop with early-stage disease, primary prevention strategies are crucial for reducing ovarian cancer-related deaths. At present, there is no effective screening of ovarian cancer.

Identifying patients at increased risk of ovarian cancer (suspicion based on family history and symptoms) is the key to prevention, early detection, and, ultimately, improving overall survival of ovarian cancer. In BRCA1 and BRCA2 germline mutation carriers, surgical removal of the fallopian tubes and ovaries has been demonstrated to reduce the risk of developing, and dying from, ovarian cancer. Although it is not very easy to perform BRCA mutation tests in India because of accessibility and the cost involved, those with BRCA1 mutations have a 39–46% lifetime risk of ovarian cancer, those with BRCA2 mutations have a 10–27% risk, and up to 24% of those with Lynch syndrome will develop ovarian cancer. Also the index case has to be present at the time of evaluation [5, 6].

If BRCA mutations or Lynch syndrome is identified in those patients who are able to give proper history and are able to undergo genetic screening, the National Comprehensive Cancer Network (NCCN) recommends removal of both fallopian tubes and ovaries between the ages of 35 and 40, based on the particular mutation carried [7].

Fallopian Origin of Ovarian Cancer

Research data and analysis published over the past 10 years have concluded that most “ovarian cancers,” and more specifically the high-grade serous carcinoma (HGSC)

subtype of ovarian cancer, actually could originate in the fallopian tube. This tubal origin of ovarian cancer hypothesis has gained momentum because they identified pre-invasive lesions in the fallopian tubes of high-risk patients undergoing prophylactic salpingo-oophorectomy as risk-reducing surgery. Distal fimbriae end of the fallopian tubes closer to the ovary has been considered as primary precursor of high-grade serous carcinoma. A step-wise transformation from normal epithelium to a lesion with the ability to invade and metastasize has been demonstrated within the fallopian tube [8].

Primary prevention could be considered a strategy to decrease the mortality from ovarian cancer, not only in women at high risk but also at low risk. Thus, bilateral salpingectomy with ovarian conservation was proposed as a “middle-ground” method of primary prevention, with the benefit of removing potential tissue of origin and without the risks of surgical menopause. Once childbearing was over, women at high risk could undergo bilateral oophorectomy at a later date. Ovarian cancer risk-reducing bilateral salpingo-oophorectomy remains the recommended standard of care for high-risk women. Bilateral salpingectomy is also suggested for low-risk women, at the time of other benign gynecologic surgeries like tubal ligation, laparoscopy for ovarian cyst, pelvic pain, etc., as a primary preventive strategy.

Some studies have shown a risk reduction in ovarian cancer in women with bilateral prophylactic salpingectomy. While evidence on how many gynecologists perform opportunistic salpingectomy is not there, there is increasing practice of doing salpingectomy during hysterectomy. Opportunistic salpingectomy for sterilization purposes, although expanding, appears to be less common. Operative and perioperative complications like blood transfusions, hospital stay and readmissions were not changed with the addition of salpingectomy either at time of hysterectomy or for sterilization. Additional operating room time was 16 min with hysterectomy and 10 min for salpingectomy for sterilization. Short-term studies of the consequences of salpingectomy on ovarian function indicate no difference between women undergoing hysterectomy alone and hysterectomy with salpingectomy, but no long-term data exist [9].

The estimated risk reduction for ovarian cancer for any individual undergoing opportunistic salpingectomy is up to 50%. Although this seems like an appreciable benefit, it must be tempered with a reminder that women at population risk of ovarian cancer have only a 1:70 or 1.4% lifetime risk. The other significant benefits of opportunistic salpingectomy, along with the risk reduction, are the ease and speed of the procedure, the rarity of complications, the convenience of removing the entire specimen, and the fact that surgical removal is theoretically the only way to permanently reduce the risk of ovarian cancer. In some

studies, bilateral tubal ligation without salpingectomy has also been associated with decreased risk. In spite of this, it is not known whether salpingectomy is more beneficial than tubal ligation. Fallopian tubes should be removed when a convenient opportunity arises, but extensive surgery should not be attempted just for that purpose. Whenever surgery is performed in high-risk women, the pathologic processing of specimens should include microsectioning the ovaries and tubes, with special attention to the fimbriae. The pathologic specimen processing in low-risk women should include representative sections of the tube, any suspicious lesions, and entire sectioning of the fimbriae [10].

The American College of Obstetricians and Gynecologists (ACOG) released a statement saying that salpingectomy should be considered for low-risk patients, but there was a clear instruction that the approach—open or laparoscopic, to pelvic surgery, hysterectomy, or sterilization should not change simply to increase the chances of completing bilateral salpingectomy. British Columbia Ovarian Cancer Research Group program, instituted in 2010, recommended performing opportunistic salpingectomy with benign hysterectomy or in lieu of bilateral tubal ligation for permanent contraception [5, 9].

The Counterargument

Data obtained from the Nurses’ Health Study suggested that oophorectomy before age 47.5 years may be associated with increased risk of death from other causes, such as cardiovascular disease. Prophylactic salpingectomy is supposed to have a theoretical 50% risk reduction in ovarian cancer. But the actual permanent ovarian cancer risk reduction with salpingectomy is not entirely clear taking into consideration the long-term effect of salpingo-oophorectomy [1].

The optimal timing of such prophylactic salpingectomy is not clear both in high-risk and in low-risk population, as the time span and age group during which the ovaries are susceptible to induction of cancer from the fallopian tubes are not established. A bilateral salpingectomy if performed at 30 years, after the child bearing is over, should be more effective at risk reduction than the same surgery at age 60 years. However, the relationship between time and risk reduction has not been studied amply. We also have to consider that there are other more commonly accepted interventions associated with ovarian cancer risk reduction, like contraceptive pills and breastfeeding for prolonged time. It is also not known how salpingectomy and oral contraceptive pill use interact with one another in risk reduction, and whether there will be compounded effect of both in the same patient [5, 7].

Another side of the coin is whether salpingectomy should be used instead of tubal ligation as it will ensure “two birds with one stone” approach to sterilization and risk reduction. Caution should be exercised when choosing salpingectomy over tubal ligation for sterilization, because of the inability to reverse salpingectomy and the patient should be thoroughly counseled and consent obtained.

Summary

Women who have known BRCA1 or BRCA2 germline mutations should be counseled regarding bilateral salpingo-oophorectomy, immediately after completion of childbearing, as the best strategy for reducing their risk of developing ovarian cancer. If the patient is reluctant, they should be counseled regarding risk-reducing salpingectomy when childbearing is complete followed by oophorectomy in the future, although the safety of this approach has not been studied. Thorough pathological evaluation by microsectioning of the ovaries and fallopian tubes (especially the fimbriae) is crucial. For women at average risk of ovarian cancer, risk-reducing salpingectomy should also be discussed and considered with patients at the time of any abdominal or pelvic surgery, hysterectomy, or tubal ligation.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest in this article.

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