Prophylactic Oophorectomy: Yes/No Risk vs Benefits

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INTRODUCTION

The removal of normal ovaries in healthy women is often indicated to reduce the risk of developing ovarian cancer (OC) in the future. They may be genetically at high risk of developing ovarian or breast cancer [most commonly those with BRCA1 and BRCA2 (Breast Cancer genes 1 and 2) mutations or those with a strong family history]. The second group are those who are not seen as high risk, that are having a hysterectomy for a benign condition, and removal of the ovaries is performed opportunistically to reduce any background risk of developing OC later in life.

PROPHYLACTIC OOPHORECTOMY

The main advantage of prophylactic oophorectomy is the reduction in the risk of ovarian, fallopian tube, and primary peritoneal cancer; others are for the treatment of severe premenstrual syndrome (PMS) or endometriosis. Any risks associated with early surgical menopause can be prevented with the use of hormone replacement therapy. The screening program for OC is still not effective.

OC RISK REDUCTION

In OC, the majority of cases present with incurable disease, then the rationale for removing the ovaries when the organs are deemed obsolete appears sensible. It has therefore been estimated that 1,000 cases of OCs could be prevented each year if every woman over the age of 40 undergoing hysterectomy had a prophylactic bilateral salpingo-oophorectomy (BSO) at the time of surgery.

The lifetime risk of developing OC in the general population is approximately 2%. The incidence of OC increases after menopause, with the peak incidence in those aged 60 to 64 years.

HIGH-RISK WOMEN

Women who have a first-degree relative diagnosed with OC are thought to have a three- to fourfold risk of developing OC, and some have advocated prophylactic oophorectomy in those with two or more first- or second-degree relatives affected. The BRCA mutations are currently the most recognized mutation contributing toward carcinogenesis, and genetic testing should be considered in high-risk families. High-risk families include those that have an affected family member of breast cancer diagnosed before the age of 50, cancer in both breasts, breast and concurrent OC, multiple breast cancer, a male affected with breast cancer, Ashkenazi Jewish ethnicity, or a family member diagnosed with two or more primary types of BRCA1 or BRCA2 related cancers. Women who are known to have a BRCA1 or BRCA2 mutation have a risk of developing OC by the age of 70 of between 40–59 and 16.5–18% respectively. Bilateral salpingo-oophorectomy has been shown to be associated with an 80% reduction in the risk of ovarian, fallopian tube, or peritoneal cancer and a 77% reduction in all-cause mortality. Women with hereditary nonpolyposis colorectal cancer or Lynch syndrome who have a defect in mismatch repair genes have a 6.7% lifetime risk of developing OC compared with approximately 2% in the general population. It could therefore be argued that only those with a known genetic mutation should be offered prophylactic oophorectomy. However, as only 10% of patients with OC have a family history of the disease and in those, known genetic mutations account for less than 50% and 5% of those that subsequently develop OC would be targeted by this approach. Environmental exposures and ageing can cause an increased risk of OC.

ABSENCE OF EFFECTIVE OC SCREENING

At present, there is no effective screening program available.

BREAST CANCER RISK REDUCTION

Performing oophorectomy is also thought to be beneficial by reducing breast cancer risk and breast cancer.
recurrence. In those with BRCA1 and BRCA2 mutation, performing prophylactic BSO in women before the age of 50 has been shown to reduce the risk of breast cancer by 53 to 56 and 46% respectively.

**BENEFITS UNRELATED TO CANCER RISK**

Benefits include avoiding the need for repeat operation due to the development of adnexal pathology or pain, although reoperation rates have been reported as low as 2.75%. Even when BSO has been performed, ovarian remnant syndrome is possible, with a higher frequency in those with endometriosis. Several reports of malignant transformation within the ovarian remnant, although rare, are known.

Benign gynecologic conditions, such as severe endometriosis, pelvic inflammatory disease, and PMS are also relieved.

**SEVERE CYCLICAL MOOD CHANGE**

In some patients, severe depressive symptoms occur secondary to circulating levels of estrogen and progesterone. Postnatal depressive symptoms are also reported; the patients are often extremely intolerant to progesterone administration.

**DISADVANTAGES**

The argument against prophylactic oophorectomy in low-risk populations is due to the opinion that the benefits of oophorectomy are outweighed by the increase in the risk of cardiovascular disease, osteoporosis and hip fracture, and neuropsychological conditions. It has been suggested that the risk of death from OC, which accounts for 15,000 deaths annually in the United States, should be balanced against the risk of deaths caused by cardiovascular disease (350,000) and hip fractures (66,000) respectively.

**OC RISK IS LOW**

In comparison to other cancers in females, the risk of OC is relatively low. Oral contraceptive pill is known to be protective by reducing the risk by a third with continued use for 5 to 9 years and reducing the risk by almost 50% with continued used for up to 15 years in duration.

**MENOPAUSAL SYMPTOMS AND POSTMENOPAUSAL HORMONE PRODUCTION**

Several studies have demonstrated that despite the significant decrease in estrogen levels after menopause, postmenopausal ovaries still remain physiologically active and continue the production of androgen and small amounts of estrogen. The climacteric ovary is thought to produce 40% of total testosterone and 20% of androstenedione. Furthermore, this production is thought to continue for at least 10 years. These androgens are converted to estrone peripherally by skin, muscle, and fat.

Vaginal dryness and discomfort during intercourse may result from early surgical menopause in premenopausal women, reduction of testosterone may directly impact on the libido, sexual desire, or even the orgasmic response.

**MENOPAUSE HEALTH RISKS**

**Cardiovascular Disease and Cancer**

There is conflicting evidence in observational studies. However, most studies appear to demonstrate increased risk in those receiving oophorectomy compared with those with ovarian conservation. Data from a cohort study on over 10,000 postmenopausal women found that the risk of ischemic heart disease was greater in those with oophorectomy before the age of 45 compared with spontaneous premature ovarian failure.

**OSTEOPOROSIS AND HIP FRACTURE**

Postmenopausal women who had BSO on average 14 years after natural menopause with 54% more osteoporotic fractures is those with BSO compared with expected women. This is further evidence that the androgen production of postmenopausal ovaries appears to be protective. Conversely to this, there is good evidence to suggest that there is no significant difference in bone loss or fracture risk between postmenopausal women with or without ovaries.

**COGNITIVE FUNCTION, DEMENTIA, AND SEVERE DEPRESSIVE DISORDERS**

Studies have found significant association of oophorectomy (unilateral and bilateral) with Parkinsonism (although not Parkinson's disease), dementia, or cognitive impairment compared with age-matched referent women [hazard ratio (HR) 1.68, 95% confidence interval (CI) 1.06–2.67 and HR 1.47, 95% CI 1.13–1.90 respectively]. This risk appeared to increase in association with earlier age of surgery.

**CONCLUSION AND RECOMMENDATIONS**

The risks and benefits should be carefully balanced and be decided upon in a personalized manner. The replacement of estrogen in those before the age of 50 is widely advocated with positive impact on cardiovascular health and osteoporotic risk and minimal increase in the risk of breast cancer.
The majority of OCs originate from the fallopian tube. Bilateral salpingectomy should be performed in all cases irrespective of ovarian conservation. This has been proposed as a prophylactic procedure in high-risk women wishing to preserve their ovaries. Further research is required in this field.

BIBLIOGRAPHY


