Review article

OOPHORECTOMY & ITS ROLE IN BREAST CANCER RISK REDUCTION

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ABSTRACT

An oophorectomy is when a surgeon removes one or both ovaries. The ovaries are the reproductive glands in women that make hormones to control the menstrual cycle and promote bone and heart health. Ovaries also contain and help grow eggs that can lead to pregnancy. Owing to the significant breast cancer risk associated with BRCA1 or BRCA2 mutations, women with these mutations have several options available to them by which to reduce the risk of breast cancer. These include surgical (prophylactic mastectomy and prophylactic oophorectomy) and medical (chemoprevention) options. The breast cancer risk reductions associated with these options range from a 90% risk reduction associated with prophylactic mastectomy to approximately 50% with oophorectomy or tamoxifen. This article reviews the efficacy of prophylactic oophorectomy for the prevention of breast cancer in BRCA1 and BRCA2 mutation carriers. The predictors of uptake of the preventive surgery will be discussed, in addition to the psychosocial implications of the surgery.

Anatomy

Structure

The ovaries are considered the female gonads.[2] Each ovary is whitish in color and located alongside the lateral wall of the uterus in a region called the ovarian fossa. The ovarian fossa is the region that is bounded by the external iliac artery and in front of the ureter and the internal iliac artery. This area is about 4 cm x 3 cm x 2 cm in size.[3][4] The ovaries are surrounded by a capsule, and have an outer cortex and an inner medulla.[4] The capsule is of dense connective tissue and is known as the tunica albuginea.[5] Usually, ovulation occurs in one of the two ovaries releasing an egg each menstrual cycle. The side of the ovary closest to the fallopian tube is connected to it by infundibulopelvic ligament,[3] and the other side points downwards attached to the uterus via the ovarian ligament. Other structures and tissues of the ovaries include the hilum.

Ligaments

The ovaries lie within the peritoneal cavity, on either side of the uterus, to which they are attached via a fibrous cord called the ovarian ligament. The ovaries are uncovered in the peritoneal cavity but are tethered to the body wall via the suspensory ligament of the ovary which is a posterior extension of the broad ligament of the uterus. The part of the broad ligament of the uterus that covers the ovary is known as the mesovarium.[4] The ovarian pedicle is made up part of the fallopian tube, mesovarium, ovarian ligament, and ovarian blood vessels.[6]

Microanatomy

The surface of the ovaries is covered with membrane consisting of a lining of simple cuboidal-to-columnar shaped mesothelium,[7] called the germinal epithelium. Micrograph of the ovarian cortex from a rhesus monkey showing several round follicles embedded in a matrix of stromal cells. A secondary follicle sectioned through the nucleus of an oocyte is at the upper left, and earlier stage follicles are at the lower right. The tissue was stained with the dyes hematoxylin and eosin. The outer layer is the ovarian cortex, consisting of ovarian follicles and stroma in between them. Included in the follicles are the cumulus oophorus, membrana granulosa (and the granulosa cells inside it), corona radiata, zona pellucida, and primary oocyte. Theca of follicle, antrum and liquor folliculi are also contained in the follicle. Also in the cortex is the corpus luteum derived from the follicles. The innermost layer is the ovarian medulla.[8] It can be hard to distinguish between the cortex and medulla, but follicles are usually not found in the medulla. Follicular cells are flat epithelial cells that originate from surface epithelium covering the ovary. They are surrounded by granulosa cells that have changed from flat to cuboidal and proliferated to produce a stratified epithelium. The ovary also contains blood vessels and lymphatics.[9]
Physiology & Function

At puberty, the ovary begins to secrete increasing levels of hormones. Secondary sex characteristics begin to develop in response to the hormones. The ovary changes structure and function beginning at puberty.[1] Since the ovaries are able to regulate hormones, they also play an important role in pregnancy and fertility. When egg cells (oocytes) are released from the Fallopian tube, a variety of feedback mechanisms stimulate the endocrine system which cause hormone levels to change.[10] These feedback mechanisms are controlled by the hypothalamus and pituitary gland. Messages from the hypothalamus are sent to the pituitary gland. In turn, the pituitary gland releases hormones to the ovaries.

Gamete production

The ovaries are the site of production and periodical release of egg cells, the female gametes. In the ovaries, the developing egg cells (or oocytes) mature in the fluid-filled The process of ovulation and gamete production, oogenesis, in a human ovary. Follicles. Typically, only one oocyte develops at a time, but others can also mature simultaneously. Follicles are composed of different types and number of cells according to the stage of their maturation, and their size is indicative of the stage of oocyte development.[11]:833 When the oocyte finishes its maturation in the ovary, a surge of luteinizing hormone secreted by the pituitary gland stimulates the release of the oocyte through the rupture of the follicle, a process called ovulation.[12] The follicle remains functional and reorganizes into a corpus luteum, which secretes progesterone in order to prepare the uterus for a potential implantation of the embryo.[11]:839

Hormone secretion

At maturity, ovaries secrete estrogen, androgen,[13][14] inhibit, and progesterone.[15][16][1] In women before menopause, 50% of testosterone is produced by the ovaries and released directly into the bloodstream. The other 50% of testosterone in the bloodstream is made from conversion of the adrenal pre-androgens (DHEA and androstenedione) to testosterone in other parts of the body. Estrogen is responsible for the appearance of secondary sex characteristics for females at puberty and for the maturation and maintenance of the reproductive organs in their mature functional state. Progesterone prepares the uterus for pregnancy, and the mammary glands for lactation. Progesterone functions with estrogen by promoting menstrual cycle changes in the endometrium.[medical citation needed][3]

Ovarian aging

As women age, they experience a decline in reproductive performance leading to menopause. This decline is tied to a decline in the number of ovarian follicles. Although about 1 million oocytes are present at birth in the human ovary, only about 500 (about 0.05%) of these ovulate, and the rest are wasted. The decline in ovarian reserve appears to occur at a constantly increasing rate with age,[17] and leads to nearly complete exhaustion of the reserve by about age 52. As ovarian reserve and fertility decline with age, there is also a parallel increase in pregnancy failure and meiotic errors resulting in chromosomally abnormal conceptions.

The ovarian reserve and fertility perform optimally around 20–30 years of age.[18] Around 45 years of age, the menstrual cycle begins to change and the follicle pool decreases significantly.[18] The events that lead to ovarian aging remain unclear. The variability of aging could include environmental factors, lifestyle habits or genetic factors.[18] Women with an inherited mutation in the DNA repair gene BRCA1 undergo menopause prematurely,[19] suggesting that naturally occurring DNA damages in oocytes are repaired less efficiently in these women, and this inefficiency leads to early reproductive failure. The BRCA1 protein plays a key role in a type of DNA repair termed homologous recombinational repair that is the only known cellular process that can accurately repair DNA double-strand breaks. Titus et al.[20] showed that DNA double-strand breaks accumulate with age in humans and mice in primordial follicles. Primordial follicles contain oocytes that are at an intermediate (prophase I) stage of meiosis. Meiosis is the general process in eukaryotic organisms by which germ cells are formed, and it is likely an adaptation for removing DNA damages, especially double-strand breaks, from germ line DNA (see Meiosis and Origin and function of meiosis).[citation needed] Homologous recombinational repair is especially promoted during meiosis. Titus et al.[20] also found that expression of 4 key genes necessary for homologous recombinational repair of DNA double-strand breaks (BRCA1, MRE11, RAD51 and ATM) decline with age in the oocytes of humans and mice. They hypothesized that DNA double-strand break repair is vital for the maintenance of oocyte reserve and that a decline in efficiency of repair with age plays a key role in ovarian aging. A variety of testing methods can be used in order to determine fertility based on maternal age. Many of these tests measure levels of hormones FSH and GnRH. Methods such as measuring AMH (anti-mullerian) hormone levels, and AFC (antral follicle count) can predict ovarian aging. AMH levels serve as an indicator of ovarian aging since the quality of ovarian follicles can be determined.[21]

The history behind the procedure

The relationship between breast cancer and the presence of functional ovaries was first observed by a British doctor, Thomas William Nunn. He reported breast cancer regression in a woman 6 months after she had reached menopause. Based on Mr. Nunn's observation, a German surgeon, Albert Schinzinger, was the first to propose removal of the ovaries as a potential therapy for breast cancer. This procedure was subsequently done for the first time in 1895 by a British physician, George Thomas Beatson. While some success was reported, it was largely unopposed at first, because it was associated with a high degree of morbidity. It was not until the mid 20th century that large oophorectomy trials focusing on its role in breast cancer were studied and reintroduced into the mainstream of breast cancer treatment. Studies by reputable bodies, such as the Early Breast Cancer Trialist's Collaborative Group, showed compelling evidence for the procedure. These studies suggested that the removal of the ovaries had a large positive effect on disease-free survival as well as on the overall survival of patients with early breast cancer. Advancements in medicine, and our understanding of breast cancer, however, has affected the practice of oophorectomy. These advancements include using chemotherapy, targeting hormone receptors and alternative ways to suppress ovarian function without removal of key genes.

Types of oophorectomy

The types of oophorectomy procedures in a female:

Bilateral oophorectomy is removal of both ovaries.

Unilateral oophorectomy is removal of only one of the ovaries.
Other surgical procedures that may be performed

Hysterectomy is the removal of a woman’s uterus. The uterus is a pear-shaped organ in the lower abdominal (pelvic) area where a baby grows during pregnancy.

Salpingectomy is the removal of one or both fallopian tubes, which connect the ovaries to the uterus. Salpingectomy is often combined with oophorectomy. If one fallopian tube is removed with one ovary, the surgery is a unilateral salpingo-oophorectomy. If both fallopian tubes are removed with both ovaries, it is a bilateral salpingo-oophorectomy.

Indication of oophorectomy

A surgeon may remove one or both of your ovaries for several reasons, including:

- A disease known as endometriosis, when cells from inside the womb (uterus) travel and grow elsewhere.
- Benign (non-cancerous) growths known as cysts.
- Preventative surgery for patients with a high risk of cancer of the breast or ovaries.
- Cancer of the ovary.
- A condition known as torsion of the ovary. This condition happens when the ovary twists around the blood supply, causing severe pain.
- An infection of the ovary or the area around it, also known as pelvic inflammatory disease (PID) or a tubo-ovarian abscess (TOA).

Women who possess BRCA1 and BRCA2 genetic mutations have a greater risk of developing ovarian and breast cancer. Those who have completed their families and have a genetic predisposition to the development of these malignant conditions are prime candidates for the procedure. It may also be performed prophylactically in those who have a strong family history of ovarian and breast cancer. Studies show that the risk of developing breast cancer in women with a BRCA mutation may be halved by bilateral oophorectomy. The chances of developing ovarian cancer in such women may be reduced by up to 90% by this procedure. It is important to note that the total risk varies depending on several factors, such as the lifestyle choices of the women (including their weight management and alcohol consumption), and their family history. Hence, oophorectomy may be of immense benefit in some women, but not in others. In the latter, the risks associated with the procedure and the possible side effects outweigh the benefit due to the reduction in cancer propensity. While the surgical procedure is generally safe, the associated risks include injury to internal organs, intestinal blockage and infection. Moreover, the premature reduction of sex hormones may lead to problems, such as osteoporosis (or bone thinning) and an increased risk of heart disease.

Procedures of the operation

Abdominal oophorectomy (open oophorectomy) is the removal of the ovaries through a five to seven inch incision in the lower part of your belly. The incision may be vertical or horizontal. A horizontal incision (bikini cut) is placed very low on the abdomen so it is not easily visible. Open surgery allows your doctor to directly see and access the surgical area. Open surgery generally involves a longer recovery and more pain than minimally invasive surgery. Open surgery requires a larger incision and more cutting and displacement of muscle and other tissues than minimally invasive surgery. Despite this, open surgery may be a safer or more effective method for certain patients.

Laparoscopic oophorectomy is the removal of the ovaries and fallopian tubes through several small incisions in your abdomen. Your doctor inserts a small tube fitted with a special camera and other surgical instruments through the small incisions to remove the ovaries. The camera transmits pictures of the inside of your body to a video screen. Your doctor sees the inside of your abdomen on the screen while performing surgery. Minimally invasive surgery generally involves a faster recovery and less pain than open surgery. This is because it causes less trauma to tissues and organs. A vaginal approach can also be performed, especially when combined with hysterectomy.

Types of anesthetics that may be used

General anesthesia is generally a combination of intravenous (IV) medications and gases that put you in a deep sleep. You are unaware of the procedure and do not feel any pain. You may also have a peripheral nerve block infusion in addition to general anesthesia. A peripheral nerve block infusion is an injection or continuous drip of a liquid anesthetic. The anesthetic flows through a tiny tube inserted near your surgical site to control your pain during and after surgery.

Regional anesthesia is also known as a nerve block. It involves injecting an anesthetic around certain nerves to numb a large area of the body. You will likely have sedation with regional anesthesia to keep you relaxed and comfortable.

Risks and complications of the procedure

Oophorectomy is a generally safe procedure that carries a small risk of complications, including infection, intestinal blockage and injury to internal organs. The risk of complications depends on how the procedure is performed. But more concerning is the impact of losing the hormones supplied by your ovaries. If you have yet to undergo menopause, oophorectomy causes early menopause. Early menopause carries many risks, including:

Reducing risk of complication

- Following activity, dietary and lifestyle restrictions and recommendations before, during and after surgery or treatment
- Informing the patient is nursing or there is any possibility that may be pregnant
- Losing weight if there is overweight. This will help to keep patient as healthy as possible and may reduce risk of heart disease and osteoporosis.
- Notifying doctor immediately of any concerns after surgery, such as bleeding, fever, increase in pain, or wound redness, swelling or drainage
- Stopping smoking. This can help reduce the risk of osteoporosis and heart disease.
- Taking medications exactly as directed

Managing side effects of prophylactic oophorectomy

Non-hormonal treatments

The side effects of oophorectomy may be alleviated by medicines other than hormonal replacement. Non-hormonal bisphosphonates (such as Fosamax and Actonel) increase bone strength and are available as once-a-week pills. Low-dose selective serotonin抑制 agents may also be useful for bladder and intestinal issues. Additionally, low-dose aspirin, fish oil, statins, proton pump inhibitors, and a general recommendation to eat a Mediterranean diet and exercise regularly can help to reduce the risk of complications.
with Lynch syndrome, might also consider this procedure. Mutations that increase the risk of ovarian cancer, including those may consider this procedure.

ovarian cancer and other cancers who have completed childbearing risk of breast cancer and ovarian cancer due to an inherited mutation Consideration of prophylactic oophorectomy

· Memory problems

· Depression

· Loss of sexual drive

· Memory loss

· Vaginal dryness

· Hot flashes

menopause can cause (19) symptoms after surgery. In addition to no longer having periods, considering having children, it is important to be prepared for control the menstrual cycle. Removing both ovaries will cause  in combination with mastectomy.[45] This result can probably be generalized to other women at high risk in whom short-term (i.e., one- or two-year) treatment with estrogen for hot flashes may be acceptable.

Oophorectomy impact on chances of fertility

Removing one ovary will not significantly change your chances of becoming pregnant, assuming your other ovary and fallopian tube are working normally. Removing both tubes and ovaries will mean that the person will no longer be able to become pregnant on their own. Young women who are told they need to undergo removal of both tubes and ovaries should see an infertility doctor to talk about storing eggs before the procedure.[23]

Relation of oophorectomy to menopause

Ovaries produce estrogen and progesterone, both of which help control the menstrual cycle. Removing both ovaries will cause menopause to begin immediately. It is important to be aware that this will happen before the procedure. Even if patient is no longer considering having children, it is important to be prepared for symptoms after surgery. In addition to no longer having periods, menopause can cause (19)

· Hot flashes

· Vaginal dryness

· Depression

· Memory loss

· Loss of sexual drive

· Memory problems

· Osteoporosis

Consideration of prophylactic oophorectomy

Prophylactic oophorectomy is usually reserved for those with:

Inherited gene mutations. People with a significantly increased risk of breast cancer and ovarian cancer due to an inherited mutation in the BRCA1 or BRCA2 gene — two genes linked to breast cancer, ovarian cancer and other cancers who have completed childbearing may consider this procedure. People with other inherited gene mutations that increase the risk of ovarian cancer, including those with Lynch syndrome, might also consider this procedure.

Strong family history. Prophylactic oophorectomy may also be recommended if you have a strong family history of breast cancer and ovarian cancer but no known genetic alteration. It might also be recommended if you have a strong likelihood of carrying the gene mutation based on your family history but choose not to proceed with genetic testing.[15]

Role of oophorectomy in breast cancer risk reduction

Clinical genetic testing for BRCA1 and BRCA2 mutations has been available since 1995. Based on a large combined analysis, for women who are identified as having a mutation in BRCA1 the risk of breast cancer is 65% and the risk of ovarian cancer is 39%; for women with a BRCA2 mutation, the risk for breast cancer is 45% and the risk for ovarian cancer is 11% [1]. These cancer risks can be compared with the general population risks of 11 and 1.4% for breast and ovarian cancer, respectively. In addition to these increased risks, women with BRCA1 or BRCA2 mutations are often diagnosed at younger ages than women in the general population. There are differences in the breast cancer phenotypes observed in BRCA1 compared with BRCA2 mutation carriers. Estrogen receptor status has been demonstrated to be different in these two groups of women. Only 10–24% of BRCA1-associated breast cancers are ER-positive, compared with 65-79% of BRCA2-associated breast cancers [2,3]. This may have implications for the ways in which BRCA breast cancers are treated and the effectiveness of breast cancer risk-reduction strategies.

Prophylactic salpingo-oophorectomy

A prophylactic salpingo-oophorectomy (PSO) involves the removal of both the ovaries and fallopian tubes. It is important that the fallopian tubes are removed since they have become recognized as an important site of occult cancer in BRCA1 and BRCA2 mutation carriers who have undergone prophylactic oophorectomy [10-13]. Currently, PSO is the most effective option available to women with BRCA1 or BRCA2 mutations by which to prevent ovarian cancer [8,14]. Although it was recognized that PSO would reduce the risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers, it was unclear if the procedure would also reduce the risk of breast cancer in this group of high-risk women. In 2002, the first two studies investigating the breast cancer risk reduction associated with prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers were reported [8,15]. Kauff et al. followed 170 BRCA1 and BRCA2 mutation carriers over the age of 35 years for a mean time of 24.2 months [15]. Of the 98 women who underwent PSO, three (3%) developed breast cancer compared with eight of 72 women (11%) who chose surveillance. Similar findings were reported by Rebbeck et al. in a retrospective study of 99 women who had undergone PSO compared with 142 matched controls [8]. The follow-up period was greater than 8 years. Of the 99 women who had undergone PSO, 21 (21%) developed breast cancer compared with 60 (42%) in the control group (hazard ratio [HR] = 0.47; 95% CI: 0.29–0.77). This suggested that PSO was associated with a 53% breast cancer risk reduction. In both of these early studies, there were no specific analyses undertaken to examine the effectiveness of PSO in the prevention of breast cancer specifically for BRCA1 versus BRCA2. In 2005, Eisen et al. presented a large, international, retrospective study of 1439 women with breast cancer and 1866 matched controls [6]. They reported that a previous history of oophorectomy was associated with a significant 56% reduction in the breast cancer risk for BRCA1 mutation carriers (odds ratio [OR] = 0.44; 95% CI: 0.29–0.66) and a 46% risk reduction for BRCA2 mutation carriers (OR = 0.57; 95% CI: 0.28–1.15). The protective effect was evident for
15 years post-oophorectomy. This study suggested that PSO may be more effective in preventing breast cancer in BRCA1 mutation carriers compared with BRCA2 mutation carriers. In contrast to this finding, Kauff et al. reported on 579 women without breast cancer (360 BRCA1 and 229 BRCA2) in a prospective follow-up study [7].

Women self-selected PSO or observation. During a 3-year follow-up period, PSO was associated with a 39% breast cancer risk reduction in BRCA1 mutation carriers (HR = 0.61; 95% CI: 0.30–1.22; p = 0.16) and a 72% risk reduction in BRCA2 mutation carriers (HR = 0.28; 95% CI: 0.08–0.92; p = 0.04). These results suggested that PSO was more effective for BRCA2 mutation carriers than BRCA1 mutation carriers. Although the results of these two studies differ in the effectiveness of PSO in BRCA1 versus BRCA2 mutation carriers, they both support the hypothesis that estrogen deprivation reduces the risk of breast cancer. This has also been supported by research on tamoxifen (antiestrogen) and breast cancer risk (both bilateral and contralateral) [9,16]. All research published to date suggests that PSO is effective at reducing the risk of breast cancer in women with a BRCA1 or BRCA2 mutation (between 39 and 72%) (Table 1).

For PSO to be effective at reducing the risk of breast cancer in BRCA1 and BRCA2 mutation carriers, the procedure must be carried out at an earlier age than when breast cancers are first observed in this group of women. This suggests that the procedure should be ideally performed between 40 and 45 years of age. In addition, research has shown that the level of breast cancer risk reduction is associated with age at PSO, probably owing to the amount of estrogen production. Although women may want to wait until the onset of menopause to have a PSO because of the side effects associated with the surgery, research suggests that PSO should be carried out earlier for maximum breast cancer risk reduction. In the large, international study of BRCA1 and BRCA2 mutation carriers by Eisen et al., age at oophorectomy was found to be associated with breast cancer risk reduction [6]. Women with oophorectomy under the age of 40 years gained the greatest breast cancer risk reduction of 67% (OR = 0.33; 95% CI: 0.15–0.73; p = 0.006). Having the preventive surgery between the ages of 41 and 50 years also offered a significant breast cancer risk reduction (OR = 0.43; 95% CI: 0.25–0.72; p = 0.001). However, having the surgery after the age of 50 years did not significantly reduce a woman's breast cancer risk (OR = 0.64; 95% CI: 0.35–1.17; p = 0.14). It is unclear if there are age differences for BRCA1 mutation carriers compared with BRCA2 mutation carriers. There have been no other studies conducted with a sample size large enough to enable subanalyses on age groups. Although this study suggests that a younger age of PSO is beneficial in terms of breast cancer prevention, other issues including family planning and premature estrogen deficiency must also be considered.

other study should be considered that of 170 women who met the criteria for entry, 98 elected to undergo risk-reducing salpingo-oophorectomy at a median of 3.6 months after receiving the results of genetic testing, and 72 chose surveillance for ovarian cancer. There was no significant difference between the two groups in terms of mean age, percent age with BRCA1 or BRCA2 mutations, mean number of first- and second-degree relatives with breast, ovarian, fallopian-tube, or primary peritoneal cancer, and percentage with a history of breast cancer, systemic chemotherapy, or oral contraceptive use. More women in the salpingo-oophorectomy group than in the surveillance group (29 of 98 women [30 percent] vs. 10 of 72 women [14 percent]) had undergone bilateral mastectomy before the start of follow-up (P = 0.02). There was no significant difference in the number of women who underwent bilateral mastectomy during a mean of 24.2 months of follow-up. Complete demographic information for the two groups is summarized in Table 2 (46).

Psychosocial implications

Although PSO offers a significant breast and ovarian cancer risk reduction in BRCA1 and BRCA2 mutation carriers, there are side effects that should be considered when making decisions about breast cancer prevention. When a premenopausal woman has an oophorectomy, she is immediately placed into menopause and as a result, experiences menopausal symptoms. Although this is not the focus of this paper, the effects of premature surgical menopause on overall health need to be carefully considered. Hormone therapy (HT) is an option for women who experience menopausal symptoms. However, there has been concern that HT use would increase a woman’s risk of developing breast cancer. In a recent large, matched case-control study, Eisen et al. reported that among postmenopausal women with a BRCA1 mutation, HT was not associated with an increased risk of breast cancer [24]. Menopausal symptoms may influence psychosocial functioning in women who undergo prophylactic oophorectomy. There is limited research describing the psychosocial impact of having a prophylactic oophorectomy. Elit et al. conducted a retrospective study of 40 women who had undergone a prophylactic oophorectomy for a family history of ovarian cancer [25]. The mean age of the women at time of oophorectomy was 50 years and the mean age at the time of questionnaire completion was 55 years. Standardized psychosocial questionnaires were used to measure various psychosocial attributes. Women in the study had a good quality of life and a significant decrease in cancer risk perception as a result of the surgery. However, they experienced menopausal symptoms and compromised sexual functioning. A larger study of 846 Dutch women who had undergone prophylactic oophorectomy had similar findings [26]. Compared with gynecologic screening, women with an oophorectomy had fewer breast and ovarian cancer worries (p < 0.001) and more favorable cancer risk perception (p < 0.05). However, the oophorectomy group reported significantly more endocrine symptoms (p < 0.001) and worse sexual functioning (p < 0.05) than the screening group. The impact of PSO on cancer-related anxiety has also been studied. In an Australian study, Tiller et al. conducted a prospective study of 95 women who were initially assessed at a familial cancer clinic and followed-up 3 years later [27]. There was a higher decrease in cancer-related anxiety for women who had undergone prophylactic oophorectomy compared with those who had not (Z = −2.19; p = 0.03). The research to date suggests that PSO offers both psychosocial risks and benefits. Women generally have lower cancer risk perception and lower cancer-related anxiety. However, the sexual side effects associated with the surgery and resulting menopause are also evident. In the majority of studies that have examined psychosocial implications of PSO, the average age of subjects has been approximately 50 years, which is close to the age of natural menopause. However, PSO is generally recommended to BRCA1 and BRCA2 mutation carriers at an age younger than 50 years. Therefore, it is unclear if psychosocial implications after PSO in younger women would be the same as those reported previously. More research is needed in this area.
Table 1. Summary of studies on breast cancer risk reduction and prophylactic oophorectomy.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of carriers included</th>
<th>Mean follow-up</th>
<th>Breast cancer relative risk %</th>
<th>REF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebeck et al. (2002)</td>
<td>241 (70)</td>
<td>10.7 years (19)</td>
<td>52 (9)</td>
<td>(3)</td>
</tr>
<tr>
<td>Stolz et al. (2003)</td>
<td>162</td>
<td>11.5 years (100)</td>
<td>51 (10)</td>
<td>(1)</td>
</tr>
<tr>
<td>Barak et al. (2015)</td>
<td>148</td>
<td>Not applicable</td>
<td>61 (BRCAl)</td>
<td>(1)</td>
</tr>
<tr>
<td>Wessels et al. (2003)</td>
<td>108</td>
<td>15.1 years</td>
<td>62 (BRCAl)</td>
<td>(3)</td>
</tr>
<tr>
<td>Weiss et al. (2003)</td>
<td>297 (703)</td>
<td>20.4 months</td>
<td>27 (BRCAl)</td>
<td>(13)</td>
</tr>
<tr>
<td>Dernst &amp; Hedges (2008)</td>
<td>734</td>
<td>(2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2** Demographic characteristics of the women.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Salpingo-oophorectomy Group (n=92)</th>
<th>Ovarial Salmon Group (n=72)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the time of genetic test — y</td>
<td>47.5</td>
<td>45.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Median</td>
<td>65.5</td>
<td>62.4</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>35.9-73.9</td>
<td>56-77.7</td>
<td></td>
</tr>
<tr>
<td>Type of mutation — %</td>
<td>56 (57)</td>
<td>60 (67)</td>
<td>0.27</td>
</tr>
<tr>
<td>BRCAl</td>
<td>42 (43)</td>
<td>26 (33)</td>
<td></td>
</tr>
<tr>
<td>No. of first- or second-degree relatives with breast, ovarian, fallopian tube, or primary peritoneal cancer</td>
<td>1.64</td>
<td>1.86</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.4</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>25.70</td>
<td>26.67</td>
<td></td>
</tr>
<tr>
<td>Previous breast cancer — %</td>
<td>69 (75)</td>
<td>65 (72)</td>
<td>0.32</td>
</tr>
<tr>
<td>Mean</td>
<td>41.6</td>
<td>39.7</td>
<td>0.21</td>
</tr>
<tr>
<td>Range</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Previous chemotherapy — %</td>
<td>60 (61)</td>
<td>59 (54)</td>
<td>0.43</td>
</tr>
<tr>
<td>Mean</td>
<td>29 (30)</td>
<td>10 (14)</td>
<td>0.02</td>
</tr>
<tr>
<td>Range</td>
<td>9.9</td>
<td>6.8</td>
<td>1.00</td>
</tr>
<tr>
<td>Previous oral-contraceptive use</td>
<td>61/95 (67)</td>
<td>60/61 (66)</td>
<td>0.86</td>
</tr>
<tr>
<td>No./yrs. with data (%)</td>
<td>0.9</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Duration of surveillance before risk-reducing salpingo-oophorectomy — y</td>
<td>3.6</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>3.6</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.2-6.3</td>
<td>0.2-6.5</td>
<td></td>
</tr>
<tr>
<td>Duration of follow-up after risk-reducing salpingo-oophorectomy or start of surveillance — y</td>
<td>27.3</td>
<td>25.4</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>30.8</td>
<td>30.6</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.17-71.7</td>
<td>0.6-76.2</td>
<td></td>
</tr>
<tr>
<td>No. of women-years of follow-up</td>
<td>193</td>
<td>152</td>
<td></td>
</tr>
</tbody>
</table>

*P values were calculated with the use of Fisher’s exact test for discrete variables and the independent-sample t-test for continuous variables.

Conclusion

Prophylactic salpingo-oophorectomy is effective at preventing both breast and ovarian cancer in women with BRCA1 or BRCA2 mutations. For maximum breast cancer risk reduction, PSO should be conducted around the age of 40 years. However, older age has been shown to be associated with uptake of PSO. In addition, women with a family history of ovarian cancer, those with a BRCA1 mutation and those with a personal history of breast cancer have the highest uptake rates of PSO. As with any preventive option, there are psychosocial implications associated with the procedure; however, more research is needed in this area. Many women with BRCA1 and BRCA2 mutations are electing for a PSO. Research has shown that it significantly reduces a woman’s risk of developing breast cancer, especially if it is carried out at a young age (before 50 years of age). However, there is little research addressing the psychosocial implications of PSO on women when they are having this surgery carried out prior to menopause. Future research is needed in this area.