



Iatrogenic Menopause vs Spontaneous Menopause

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INTRODUCTION

Hysterectomy is the most common major gynecologic surgery performed in the United States, with roughly 433,000 surgeries reported in 2010.¹ Elective oophorectomy is performed in approximately 40% of women undergoing hysterectomy for benign disease. Adnexal surgery at the time of hysterectomy performed for benign indications is a part of preoperative patient counseling and has many consequences.² Bilateral salpingo-oophorectomy (BSO) is the most definitive prevention against ovarian cancer, which has a lifetime risk of 1.4%. With no screening method for ovarian cancer and poor prognosis at diagnosis, oophorectomy is crucial.³

Perimenopause, which on average lasts 3.5 years, refers to the reproductive stage immediately before menopause, includes endocrine, biological, and clinical changes, and ends in the year after the final menstrual period.⁴ Natural menopause (NM) occurs at an average age of 51 years and is the result of ovarian follicular depletion with decreases in ovarian hormone secretion resulting in very low estrogen levels and high follicle-stimulating hormone concentrations. Surgical removal of the two ovaries before the natural age of menopause is called *surgical menopause* (SM).⁵

For women with ovarian, fallopian tube, or breast carcinoma, there are often clear indications for SO. However, when no malignancies exist, the decision to retain or remove ovaries should be based on the long-term health effects. In addition to operational risks, there are adverse effects of perimenopausal oophorectomy, such as sexual dysfunction, mood disorders, anxiety, decreased cognitive function, cardiovascular effects, diabetes, increased rate of bone mineral loss, and carotid thickening.

More than 90% of hysterectomies, up to two thirds of which are performed for menstrual disorders alone, are performed for benign disease. Various studies have investigated the effects of SM on women's sexual life, demonstrating that removing the ovaries has a deleterious effect on sexual function. Few studies have stated that SM improves sexual life, whereas others have indicated that SM has no effect or is associated with deterioration. Therefore, this subject requires clarification.⁶

This editorial explores the lifesaving advantages and benefits of oophorectomy at the time of hysterectomy vs the intolerable ramifications that follow the same procedure.

PRO

The lifetime risk for developing ovarian cancer is 1 in 70, making it the fifth leading cause of cancer in women.² Unfortunately, no accurate screening tests exist for ovarian cancer; most produce false-positive results. Prognosis is poor, especially for more aggressive epithelial ovarian carcinomas, which represent 75% of all cases of ovarian cancer and are responsible for 90% of deaths of ovarian cancer.⁷ The most effective means of decreasing the burden of ovarian cancer is prophylaxis.⁸

The primary reason for oophorectomy at the time of hysterectomy is to prevent ovarian and fallopian cancer. Candidates for SM often have concerns about the effects of surgery; however, preoperative mental health and sexual function have greater impact: women with preoperative depression or sexual problems are at increased risk for experiencing moodiness and decreased libido postoperatively.⁹ Analysis of hysterectomy with BSO demonstrated that only women with preoperative depression complained of anorgasmia after the surgery.⁹ Counseling is critical in candidates for hysterectomy and BSO; therefore, physicians must be informed of all psychological risk factors in their patients.

Collaris et al¹⁰ recorded a prospective follow-up of changes in menopausal complaints after SM using weekly Greene Climacteric Scale questionnaires before and after surgery. Results showed little to no vasomotor symptoms, and anxiety and depression ratings were overall improved after total abdominal hysterectomy and BSO. This study strengthens the notion that hysterectomies can be performed to eliminate symptoms and improve quality of life.

Many publications in the past decade have tried to prove that hysterectomy negatively affects female sexual function; however, literature exists proving little significant difference between women who undergo SM vs NM. In 2015 a study comparing two groups of women who had undergone SM by hysterectomy and BSO for benign reasons or NM with intact ovaries and uterus found that the only difference based on a modified Female Sexual Function Index was lubrication (all other domains showed no significant differences).⁶ Vaginal lubrication is the easiest domain to treat.

Prophylactic oophorectomy will continue to be performed for the following indications: at hysterectomy to prevent ovarian

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cancer, to cure ovarian cycle syndrome, and in cases of endometriosis to avoid the need for further surgery for residual ovaries, which affects up to 47% of women with endometriosis who undergo hysterectomy without BSO.¹¹

Severe endometriosis is another indication to perform oophorectomy and is advocated for these patients to prevent repeat operations. The frequency of repeat surgery for ovarian pathology is reported to be twice as high in women who had retained one ovary vs two ovaries (7.6% vs 3.6%). Most of these repeat surgical procedures are performed because of pelvic pain or a pelvic mass and occur within 5 years of the hysterectomy. Women with endometriosis, pelvic inflammatory disease, and chronic pelvic pain are at higher risk of reoperation if the ovaries are retained. The risk of subsequent ovarian surgery should be weighed against the benefit of ovarian retention in these patients.¹²

Hysterectomy with BSO is regarded as definitive therapy for the treatment of endometriosis accompanied by intractable pelvic pain, adnexal masses, or multiple previous conservative surgical procedures. Based on results of a retrospective analysis of women monitored for a mean duration of 58 months after hysterectomy, ovarian conservation was associated with a 62% likelihood of recurrent symptoms and a 31% chance of requiring additional surgical treatment, illustrating the need for oophorectomy at the time of hysterectomy. In the same study, women who underwent bilateral adnexectomy had a 10% chance of recurrence of symptoms and only a 4% likelihood of additional surgery. The investigators also reported that the relative risk for recurrence of pain and additional surgery after total abdominal hysterectomy occurs more frequently with ovarian preservation compared with women who undergo ovarian removal.¹³

CON

Although during the past two decades prophylactic BSO has been considered a standard of care to prevent ovarian cancer, 300 women at low risk for developing ovarian cancer would need to be treated by prophylactic BSO, according to Larson,¹⁴ an ovarian conservationist and outcomes researcher. In other words, 300 oophorectomies have to be performed to prevent one death from ovarian cancer.

Today, those women who underwent oophorectomy have developed health consequences, including shorter life expectancy; increased risk of death from coronary heart disease (23%), lung cancer (29%), colorectal cancer (49%), and a 13% increase in all-cause mortality.¹⁵ The need to re-evaluate the benefits of preventative BSO at the time of hysterectomy in perimenopausal women has surfaced because of its debilitating repercussions.

Different studies have established that SM leads to distressing and abrupt symptoms, especially sexual dysfunction, compared with women who undergo NM.^{5,16}

BSO in a perimenopausal woman causes SM. This iatrogenic menopause has undesirable outcomes that affect approximately 75% of middle-age American women who consider sexual

activity moderately to extremely important.¹⁷ In particular, arousal, orgasm, and vaginal receptivity are damaged. Women who experience these symptoms endure pain and discomfort during sex, which affects sexual relationships and marriages.¹⁸ What further alienates these women is the failure to be sufficiently informed about the unpleasant side effects of BSO.

Androgens are essential for libido, sexual arousal, and pleasure and play a role in vaginal and clitoral function during genital sexual arousal. It has been hypothesized that decreasing androgen levels follow BSO, causing decreased sexual desire.⁶ Surgical removal of the ovary causes an abrupt, rather than gradual, decrease in ovarian sex steroid production. Compared with the intact postmenopausal ovary, which preserves minimal production (specifically of testosterone), an absolute cessation of steroid production occurs.⁵ The sudden and complete loss of all ovarian steroids causes the immediate postoperative appearances of hot flashes, vaginal dryness, mood changes, and dyspareunia, which are often more severe than in women with NM.⁵ In two cross-sectional studies, sexual function in women who had elected to undergo prophylactic SO was compared with that of women who had chosen screening; those who underwent surgery reported more vaginal dryness and dyspareunia and less pleasure and satisfaction during sexual activity. Those women who had surgery and took hormone therapy experienced significantly less severe symptoms, but hormone replacement therapy did not entirely mitigate vaginal dryness, pain with intercourse, and loss of interest in sex.⁵ According to a Cochrane review, hormone therapy had a small to moderate benefit when treating sexual dysfunction in perimenopausal and postmenopausal women.¹⁹

In another study addressing sexual dysfunction after risk-decreasing SO, the Female Sexual Function Index score was below normal values (normal = 26.55). Domains that were most affected by the procedure were desire, arousal, and satisfaction.²⁰

Evidence of the deleterious effects on mental and sexual status in women undergoing oophorectomy is abundant.^{5,20–22} When comparing hysterectomy with and without oophorectomy, Chen et al²¹ found lower scores in the domains of sexual arousal, vaginal lubrication, orgasm, sexual satisfaction, and pain.

Farahmand et al²³ proved in their 12-year cohort study that metabolic disturbances are more prevalent in those undergoing surgical menopause. The study compared the effect of menopausal types (SM and NM) on metabolic syndrome 3 years before and after menopause.

As mentioned earlier, epithelial ovarian carcinomas represent the majority and the more fatal ovarian cancer. Histopathology illustrates that serous, endometrioid, and clear cell carcinomas are derived from the fallopian tube and the endometrium and not directly from the ovary.⁷ This is in contrast to the traditional view of ovarian carcinogenesis in which ovarian surface epithelium (mesothelium) undergoes metaplastic changes leading to the different histologic types of epithelial ovarian cancer. By performing SO when patients undergo hysterectomy, the risk of

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