1 of 6



Surgical menopause: a toolkit for healthcare professionals

Key points:

- Surgical menopause (bilateral oophorectomy) is commonly undertaken during a hysterectomy to treat various medical conditions
- Menopausal symptoms can be particularly severe due to the sudden loss of ovarian function in both pre/post-menopausal women, although current evidence characterising this is limited
- Vasomotor symptoms, sexual dysfunction, increased risk of cardiovascular and osteoporotic disease and loss of fertility are some common consequences
- Libido loss can be more prominent than in a natural menopause
- HRT (Hormone Replacement Therapy) plays a significant role in managing surgical menopause, especially in women < 45 years old (provided there are no contraindications such as personal history of hormone dependant cancer)
- All women undergoing surgical menopause should have counselling and be provided with information about the hormonal consequences of surgery and the role of HRT, both before surgery and before leaving hospital, with clear communication to the primary care team.

What is surgical menopause?

Surgical menopause is the removal of both ovaries (bilateral oophorectomy) before a woman goes through biological menopause.

Menopause is a physiological state in a woman's life that occurs at the end of her natural fertility, resulting in a loss of menstrual cycles. Around the ages of 45-55 years, the ovaries stop producing mature oocytes, which in turn affects the normal menstrual cycle, leading to reduced levels of oestrogen and progesterone. Natural menopause is usually defined by at least 12 months of amenorrhea, along with various characteristics including vasomotor, psychological, and sexual symptoms². The duration and intensity of symptoms can vary significantly between patients, hence a tailored, individualised approach is recommended. Menopause usually occurs naturally, however can be induced either chemically (using pharmacological treatments) or surgically for various reasons.

Indications for surgical menopause

Bilateral oophorectomy is usually performed due to either benign or malignant underlying pathology, often at the time of hysterectomy¹. In particular, women who are carriers of the BRCA 1 or 2 mutations are at significantly higher lifetime risk of developing breast or ovarian cancer and may undergo bilateral salpingo-oophorectomy as risk reducing surgery.

In these women, add-back HRT has not been shown to diminish the risk-reducing benefit of BSO on subsequent risk of breast cancer diagnosis, but the clinical data is very limited.^{3,4} Currently, the recommendation is that after risk-reducing BSO, add-back HRT can be used until the age of an expected natural menopause. After this, non-hormonal alternatives can be used as first-line management for symptom control.

Malignant	Benign
Ovarian carcinoma: primary tumours and in women with an underlying genetic predisposition (e.g., Lynch Syndrome, BRCA1/2 mutation)	 Heavy menstrual bleeding Fibroids Endometriosis Chronic pelvic pain Heavy menstrual bleeding Recurrent ovarian cysts Gender reassignment
Other gynaecological oncologic surgery including procedures for endometrial and cervical carcinoma. Some women may undergo ovarian preservation depending on the stage of disease and patient's age	Acute pathology (rarely resulting in bilateral oophorectomy): • Adnexal torsion leading to necrosis • Ectopic pregnancy

Common consequences of surgical menopause

Symptoms of surgical menopause are generally similar to that of a natural or chemically induced menopause, with a few established differences⁵. Due to the sudden loss of ovarian function in surgical menopause, pre-menopausal women might experience more severe consequences, including increased rates of overall mortality, coronary heart disease, stroke, cognitive impairment, osteoporosis and sexual dysfunction. There is evidence to suggest that the cardiovascular risk of surgical menopause may be greater than a premature natural menopause. Some studies suggest that post-menopausal ovaries play a role in androgen production, theorising that a surgical menopause can impact libido more significantly compared to natural menopause⁶. There is limited high quality large-scale data to quantify and assess the increased risk seen in surgical menopause, in both pre/post-menopausal women. However, current evidence strongly advocates for the use of HRT to improve outcomes in women undergoing surgical menopause⁷.

Potential benefits Potential risks Reduced risk of ovarian cancer • Vasomotor symptoms: night sweats, hot flushes Reduced risk of breast and ovarian cancer Loss of fertility in susceptible women such as BRCA 1/2 carriers • Increased risk of cardiovascular disease Improvement in symptoms associated with Loss of bone density and increased risk chronic conditions such as endometriosis of osteoporosis and fractures • Sexual dysfunction including low libido, vaginal or chronic pelvic pain dryness and urogenital atrophy Recurrent urinary tract infections Change in mood and cognition including an increased risk of depression, memory loss and anxiety

Management of surgical menopause

- Use a holistic approach when counselling women, including lifestyle measures.
- Current guidelines state all women <45 years old undergoing surgical menopause should be offered HRT until age 51, unless there are contraindications to treatment such as a personal history of hormone dependant cancer.
- Oestrogen-only HRT can be used in women without a uterus (hysterectomy). Women retaining their uterus MUST receive combined Oestrogen and Progesterone combinations to reduce the risk of endometrial carcinoma.
- Further treatment or treatment in post-menopausal women should be reviewed based on symptoms.

Women should be offered treatment by menopause specialists if required, especially younger women who require long-term (>5 years) symptom management⁸.

Lifestyle interventions

- Diet, reducing caffeine and alcohol
- Exercise
- Smoking cessation
- Blood pressure management
- Optimal glucose and lipid control
- Psychological support including Cognitive Behavioural therapy

Pharmacological interventions

- HRT (either oestrogen only or combined oestrogen/ progesterone preparations): In BRCA carriers swap to non-hormonal at age 50/51yrs
- Including Tibolone (licensed for endometriosis)
- Topical vaginal oestrogen pessary/cream, vaginal DHEA
- Testosterone gel or implant
- Selective Serotonin Reuptake inhibitors (SSRIs), Clonidine or Gabapentin

Hormone Replacement Therapy (HRT)

Benefits:

- 1. Vasomotor symptom relief: HRT reduces vasomotor symptoms in most women, although symptoms may persist in younger women and require higher doses of oestrogen. Discontinuation of HRT can result in a recurrence of vasomotor symptoms.
- 2. Libido: Tibolone can be helpful for women with low libido due to some androgenic activity. It may also be used in women with endometriosis who have had a hysterectomy and bilateral oophorectomy but may have some endometriosis deposits remaining. Topical vaginal oestrogen, dehydroepiandrosterone (DHEA) and supplemental testosterone can be used to treat vaginal dryness/atrophy and reduced libido respectively if necessary.
- 3. Bone: HRT reduces the risk of osteoporotic fragility fractures and might improve muscle mass and strength^{10,11}.
- 4. Cardiovascular disease: Hormone replacement is likely to lower the long-term risk of cardiovascular disease associated with surgical menopause.
- 5. Dementia: HRT is likely to improve cognitive function and lower the risk of dementia in younger women who have had a surgical menopausal¹³.

Risk associated with HRT include2:

- 1. Venous thromboembolism: risk is increased with oral HRT but not increased from baseline with transdermal preparations. Women with an increased baseline risk (including BMI $> 30 \text{kg/m}^2$ should be offered transdermal HRT)
- 2. A perceived risk of HRT is breast cancer. However, data suggest that women <50 years on HRT do not have an increased risk of breast cancer¹⁵. A recent meta-analysis published in The Lancet suggested that women < 50 years who were postmenopausal and on HRT had an increased risk of breast cancer. The control group, of age-matched postmenopausal women, however, was inappropriate as an early menopause reduces breast cancer risk. The population for comparison should have consisted of age-matched normally cycling women¹⁶. The consensus statement issued from the BMS states that women aged < 50 years using HRT do not have an increased risk of breast cancer.</p>

For women undergoing surgical menopause due to endometriosis8:

- 1. Continued combined oestrogen/progesterone HRT is advised following hysterectomy in women who have widespread endometriosis to reduce the risk of stimulation and malignant transformation of endometrial deposits.
- Changing to estrogen only at a later date due to a better safety profile can be considered but must be balanced with the risk of reactivating endometriosis and potential malignant transformation of endometrial deposits.
- 3. HRT should be reviewed and suspended if symptoms recur.

In summary, surgical menopause can have significant consequences both short term and long term. Clear information and advice should be provided both before and after surgery to both the patient and her primary care team.

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