

藍國忠

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## Management of obesity in menopause (停經婦女肥胖的處置)

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Obesity presents a major public health challenge globally, especially for menopausal women who experience increased risks due to hormonal changes. The decline in estrogen during menopause alters fat distribution from a gynoid (hip-based) to an android (abdominal) pattern, leading to increased visceral fat and various physiological changes. Aging further complicates this, as it is linked to a reduced basal metabolic rate and a loss of muscle mass, which exacerbates fat accumulation. Factors such as physical inactivity, psychological stress, and poor dietary habits contribute to obesity.

This shift in body composition significantly heightens the risk of cardiovascular diseases and metabolic disorders. Excess weight can place additional strain on joints, raising the likelihood of osteoarthritis, while decreased muscle mass increases the risk of falls and fractures. Menopausal obesity is also associated with depression, poor sleep quality, and worsened symptoms like hot flashes, all of which detrimentally impact quality of life.

Managing menopausal obesity and its related health issues is multifaceted. Effective strategies include lifestyle interventions focused on dietary changes and physical activity. For those who struggle to achieve weight loss through these methods alone, pharmacological options such as GLP-1 receptor agonists (e.g., semaglutide) have proven effective in reducing weight and enhancing metabolic health.

Surgical options, including metabolic or bariatric surgeries like sleeve gastrectomy, are viable for patients with severe obesity or related complications, leading to significant weight loss and relief from comorbidities. Additionally, hormone replacement therapy (HRT) may alleviate menopausal symptoms; however, obese women need careful evaluation of thrombotic risks, with transdermal administration preferred to reduce these hazards.

Obstetricians and gynecologists play a crucial role in addressing obesity in menopausal women. They should offer tailored health counseling, collaborate with nutritionists, endocrinologists, and bariatric surgeons, and create comprehensive treatment plans. Early intervention and education are vital for effectively preventing and managing obesity in this population.

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## The musculoskeletal syndrome of menopause

As the ovarian production of estrogen diminishes in midlife and ultimately stops, it is estimated that more than 47 million women worldwide enter the menopause transition annually. An estimated 70% of all midlife women will experience the musculoskeletal syndrome of menopause, 25% will experience severe symptoms and 40% will have no structural findings.

The musculoskeletal syndrome of menopause includes, but is not limited to, musculoskeletal pain, arthralgia, loss of lean muscle mass, loss of bone density with increased risk of resultant fracture, increased tendon and ligament injury, adhesive capsulitis and cartilage matrix fragility with the progression of osteoarthritis.

These musculoskeletal issues can be attributed to the decline in estradiol, the most biologically active form of estrogen, which impacts nearly all types of musculoskeletal tissue including bone, tendon, muscle, cartilage, ligament and adipose. The fall in estradiol levels leads to five primary changes: an increase in inflammation, a decrease in bone mineral density leading to osteopenia/osteoporosis, arthritis, sarcopenia and a decrease in the proliferation of satellite cells (muscle stem cells).

Given the significant effects of these processes on quality of life and the associated personal and financial costs, it is important for clinicians and the women they care for to be aware of this terminology and the constellation of musculoskeletal processes for which proper risk assessment and prophylactic management are of consequence.

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## Endocrine consequences of breast cancer therapy and survivorship

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Breast cancer is currently the most common cancer globally and issues like menopausal symptoms and fertility are increasingly important. Today's lecture will address the long-term endocrine effects caused by treatment in breast cancer patients.

While chemotherapy can induce ovarian failure, Tamoxifen may trigger ovarian hyperstimulation, endometrial tissue growth, and coagulation. Aromatase inhibitors lower estradiol in postmenopausal women by blocking androgen conversion to estrogen and required strategies to prevent increased estrogen production in premenopausal women. The POSITIVE (Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer) trial and some retrospective data give some reassurance regarding the safety of interrupting therapy in the short to medium term.

Treatments for breast cancer caused by common menopausal symptoms can be worse than those experienced during natural menopause. Although hormone replacement therapy is typically not advised, non-hormonal treatments may not be as effective for symptoms like hot flashes and vulvovaginal atrophy. The contraindication of exogenous estrogens for managing menopausal symptoms raises questions warranting further debate.

By understanding and addressing these complex issues, healthcare providers can better support the long-term well-being and quality of life of breast cancer survivors.

### HIGHLIGHTS

1. Understanding the endocrine and menopausal challenge in breast cancer survivors is key to enhancing their long-term well-being and quality of life.

2. The POSITIVE trial and retrospective data provide reassurance about the short- to medium-term safety of interrupting endocrine therapy for the aim of pregnancy.

3. The contraindication of exogenous estrogens for managing menopausal symptoms in breast cancer survivors raises questions warranting further debate.

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### **Sleep disturbance associated with the menopause**

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Sleep disturbances associated with menopause are prevalent and challenging in midlife women, characterized by frequent awakenings, difficulties in sleep initiation and maintenance, and non-restorative sleep. These disturbances are often linked to hormonal changes, vasomotor symptoms (e.g., hot flashes), mood fluctuations, and anxiety. Research highlights the pivotal role of hypothalamic kisspeptin/neurokinin B/dynorphin (KNDy) neurons in regulating reproduction, thermoregulation, and sleep-wake cycles. Estrogen decline triggers hyperactivity in these neurons, contributing to sleep problems. Additionally, reduced melatonin secretion and disrupted circadian rhythms exacerbate these disturbances with age.

In terms of pharmacological treatment, hormone therapy (HT) is effective for women with vasomotor symptoms but often requires high doses for symptom control, and its use is limited by contraindications and safety concerns. Emerging treatments like elinzanetant, a neurokinin-1 and -3 receptor antagonist, have shown significant efficacy in clinical trials for managing hot flashes and sleep disturbances, offering a promising avenue for future interventions.

For non-pharmacological approaches, cognitive-behavioral therapy for insomnia (CBT-i) remains the gold standard, demonstrating substantial efficacy in improving insomnia in menopausal women. However, its implementation is hampered by limited access to trained practitioners and patient adherence. Digital CBT-i offers a scalable and effective alternative. Natural remedies, including melatonin, probiotics, and herbal supplements like soy isoflavones, are gaining popularity but require further high-quality evidence to validate their effectiveness.