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The Impact Of Menopause On The Musculoskeletal System: A Practical Overview

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Key Points

- Menopause is associated with a rapid decline in estrogen, which significantly affects bone, joint, and muscle health.
- Bone loss accelerates during the menopause transition, with up to a 10% reduction in spine bone density within the first five years after the final menstrual period.
- Menopausal hormone therapy (MHT) has been shown to be effective in preserving bone density and reducing fracture risk.
- Musculoskeletal symptoms, such as pain, stiffness, and joint discomfort are common and often underrecognized during the menopause transition, sometimes leading to misdiagnosis.
- Foundational strategies for preserving musculoskeletal health during and after menopause include lifestyle interventions such as strength training, balance exercises, and adequate protein and vitamin D intake.

Menopause represents an important phase in a woman's reproductive life, marked by the permanent cessation of menstrual periods, signalling the end of the reproductive years. In North America, the average age of onset is 50.5 years, generally occurring between the ages of 45 and 55.[1] Hormonal fluctuations and symptoms of hypoestrogenism—such as hot flashes, night sweats, mood and cognitive changes—can begin up to 10 years before menopause, during the perimenopausal or menopause transition.[1] These symptoms stem from fluctuations in sex hormones, primarily estrogen, which has receptors distributed throughout the body and impacts nearly every organ system, including the bones, joints, and muscles.[2] In this review, we will summarize the effects of hypoestrogenism on bone, joint, and muscle health during and beyond the menopause transition.

Menstrual Periods (MP) And Bone Health

Estrogen plays a critical role in regulating bone turnover, a process involving osteoclasts and osteoblasts that work within specialized cellular units to maintain bone integrity. Osteoblasts are responsible for bone formation, whereas osteoclasts drive bone resorption.[3] Estrogen suppresses bone resorption by inhibiting osteoclast function. As estrogen levels decline during perimenopause, osteoclast activity increases, leading to accelerated bone resorption, overall bone loss, and weakened bone architecture. In turn, this bone loss increases the risk of osteoporosis and fractures later in life. A rapid phase of bone loss occurs within the one- to two-year period surrounding the final menstrual period (FMP) and continues for three years thereafter.[4] During this period, the bone loss is estimated to occur at an annual rate of 1.8–2.3% at the spine and 1.0–1.4% at the hip. As a result, bone density can decline by up to 10% at the spine and 7% at the hip within the first five years following the FMP.[5] This rapid loss of bone density over a relatively short period of time makes the menopausal transition a crucial window of opportunity for optimizing bone health and implementing preventive strategies to mitigate this loss.

Although osteoporosis often remains asymptomatic, its most serious clinical outcome is fracture. The general management approach for osteoporosis in menopause aims to prevent fractures and maintain bone mineral density (BMD). This involves a combination of pharmacological and non-pharmacological strategies. Pharmacological options are based on a patient risk assessment, commonly using the

Fracture Risk Assessment Tool (FRAX) for risk stratification, and may include the use of bone-sparing medications such as bisphosphonates, receptor activator of nuclear factor kappa b (RANK)-ligand inhibitors (i.e., denosumab), and anabolic agents such as teriparatide and sclerostin inhibitors (romosozumab).[6]

Non-pharmacological management begins with a comprehensive assessment of fall risk, followed by the implementation of preventive measures. Maintaining mobility is essential, and this is best achieved through a combination of balance and muscle-strengthening exercises aiming for ≥ twice weekly, tailored to the individual's needs and physical capacity.[6]

Addressing nutritional deficiencies is also a crucial component of bone health management. Ensuring an adequate intake of calcium, with a target of 1200 mg/day, can be achieved through calcium-rich foods or supplementation.[6] Optimizing vitamin D levels is recommended, with a daily supplement of at least 400 IU/day to achieve serum 25-hydroxyvitamin D levels equal to or greater than 50 nmol/L. However, patients with vitamin D deficiency may require higher doses to reach sufficient levels.[6]

What Is The Role Of Menopausal Hormone Therapy (MHT) In Maintaining Bone Health?

There is robust data supporting the use of MHT for maintaining bone density and reducing fracture risk. MHT has been shown to increase BMD by 6% at the spine, 5% at the total hip, and 4% at the femoral neck compared to placebo.[7] In addition, studies show that MHT can prevent menopausal bone loss, with even low-dose MHT offering protection.[8] With regard to fracture risk, results from the Women's Health Initiative (WHI) study show that MHT reduces the risk of hip fracture by up to 30% and the risk of all fractures by 24%.[7]

While the Canadian-based Society of Obstetrics and Gynecology (SOGC) guidelines on menopause do not recommend using MHT primarily for bone protection, the US-based Menopause Society Guidelines do endorse its use for bone protection.[9,10]

When treating postmenopausal osteoporosis, the most recent Osteoporosis Canada guidelines recommend MHT as an alternative treatment option to bone-sparing medications for postmenopausal females aged <60 years or within 10 years of menopause who are experiencing menopausal symptoms who meet the criteria for treatment of osteoporosis.[6] However, because bone loss occurs with cessation of MHT, patients who discontinue MHT should be monitored and followed in accordance with osteoporosis management guidelines.

MP And Joint Health

Estrogen also plays a critical role in connective tissue cells, including chondrocytes within articular cartilage, and is essential for maintaining the health of joints, ligaments, and muscles.[11] The concept of "arthritis of the menopause" was first described in 1926, and more recently, the term Musculoskeletal Syndrome of Menopause has been introduced to describe the constellation of musculoskeletal signs and symptoms associated with the menopausal transition.[12,13] Polyarticular osteoarthritis (OA) is more prevalent in women over the age of 50 compared to age-matched men, suggesting a potential contributory role of estrogen in this sex-based disparity.[14] Although declining estrogen levels during menopause can contribute to the progression and worsening of OA, they are not the sole factor. Other important contributors include age, prolonged disease duration, and degenerative changes.[15]

Musculoskeletal pain is a common yet underrecognized symptom of menopause, with evidence suggesting that more than 70% of perimenopausal women are affected.[16] Aches and joint stiffness are the most frequently reported musculoskeletal symptoms during the menopausal transition; however, they may not necessarily indicate osteoarthritic disease.[17] Determining the underlying cause of joint pain in postmenopausal women can be challenging, as the menopause era coincides with a rise in the prevalence of chronic rheumatic disorders, including osteoarthritis. Addressing the patient's concern through clinical evaluation for structural damage and ruling out potential pathology is necessary, keeping in mind the role of estrogen deprivation in this population. Notably, studies suggest that up to 40% of women who present with musculoskeletal concerns during the menopause transition have no detectable structural abnormalities, and their symptoms are frequently misdiagnosed as rheumatologic or immunological conditions rather than being attributed to menopause.[16]

What Is The Role Of MHT In Maintaining Joint Health?

MHT has been shown to positively influence musculoskeletal symptoms, as demonstrated by the findings from the WHI study, which found that women receiving MHT reported a reduced incidence of new musculoskeletal concerns, including joint pain, stiffness, general aches, low back pain, and neck discomfort.[18] However, discontinuing MHT can exacerbate musculoskeletal symptoms. A cross-sectional survey of over 9,000 WHI participants revealed that those who experienced abrupt MHT withdrawal following health concerns reported a significant increase in pain and stiffness within 8 to 12 months.[19]

Although numerous studies have demonstrated a relationship between estrogen deficiency and OA, the role of MHT in improving OA symptoms and preventing disease progression remains unclear. Epidemiological evidence suggests that estrogen therapy may exert a greater impact on large joint OA compared to small joint OA.[20] While radiographic studies have indicated a protective impact of MHT on the radiographic identification of OA or its progression, a recent meta-analysis reported a higher rate of knee arthroplasty among individuals treated with MHT.[21,22] However, these findings may have been confounded by the healthy user effect, where women receiving MHT often have better access to healthcare services and are more likely to have good access to healthcare providers, are therefore more likely to be assessed for and treated for OA.

MP And Muscle Health

Estrogen is essential for maintaining skeletal muscle health, as it facilitates the proliferation, differentiation, and regeneration of muscle stem cells.[23] These stem cells, known as satellite cells, reside within skeletal muscle fibers and are vital for muscle proliferation, differentiation, and the maintenance of muscle mass and strength. Estrogen exerts its effects by binding to estrogen receptors on satellite cells, promoting their proliferation and aiding in muscle repair.[23]

Aging and menopause are associated with a progressive decline in muscle mass and function, a condition known as sarcopenia. According to the European Working Group on Sarcopenia in Older People (EWGSOP2), sarcopenia is defined as a progressive and generalized skeletal muscle disorder associated with an increased risk of adverse outcomes, including falls, fractures, physical disability, and mortality.[24] Muscle mass typically begins to decrease around the age of 30, with a further decline of 2–7% per decade, particularly accelerating after the age of 60.[25] Following menopause, muscle mass diminishes at an estimated rate of 0.6% per year.[26]

Symptoms of sarcopenia include a history of falls, gait instability, generalized weakness, decreased walking speed, and challenges in rising from a chair or climbing stairs.[24] Numerous validated screening tools exist for assessing the risk of sarcopenia. The EWGSOP2 endorses the Strength, Assistance in walking, Rise from a chair, Climb stairs, Falls (SARC-F) questionnaire, a straightforward five-item self-reported screening instrument.[25,27]

Several factors contribute to the development of sarcopenia, including inadequate nutrition, especially low protein and vitamin D intake, reduced physical activity, and hormonal shifts during the menopause transition, notably decreases in serum levels of estrogen and testosterone.[28] Additionally, comorbid conditions such as obesity may worsen muscle loss by promoting fat infiltration into muscle tissue and impairing physical function.[29]

Research demonstrates that total energy and protein consumption typically decline during the menopausal transition, underscoring the necessity of dietary optimization for muscle health.[30] Given the increased protein requirements of healthy older adults, the European Society for Clinical Nutrition and Metabolism recommends a daily intake of 1.0–1.2 g/kg body weight/day as optimal for a healthy older individual. This should be tailored according to an individual's nutritional status, physical activity level, disease status, and tolerance.[31] Physical exercise, including both aerobic and resistance training, is suggested as a non-pharmacological approach to counteract sarcopenia induced by estrogen deficiency.[32]

What Is The Role Of MHT In Maintaining Muscle Health?

The effect of MHT on sarcopenia can vary depending on the timing of its initiation during the menopause transition, though overall the research in this area remains limited. Some studies indicate that initiating MHT in early post menopause, rather than late post menopause, is linked to a substantial increase in the number of muscle

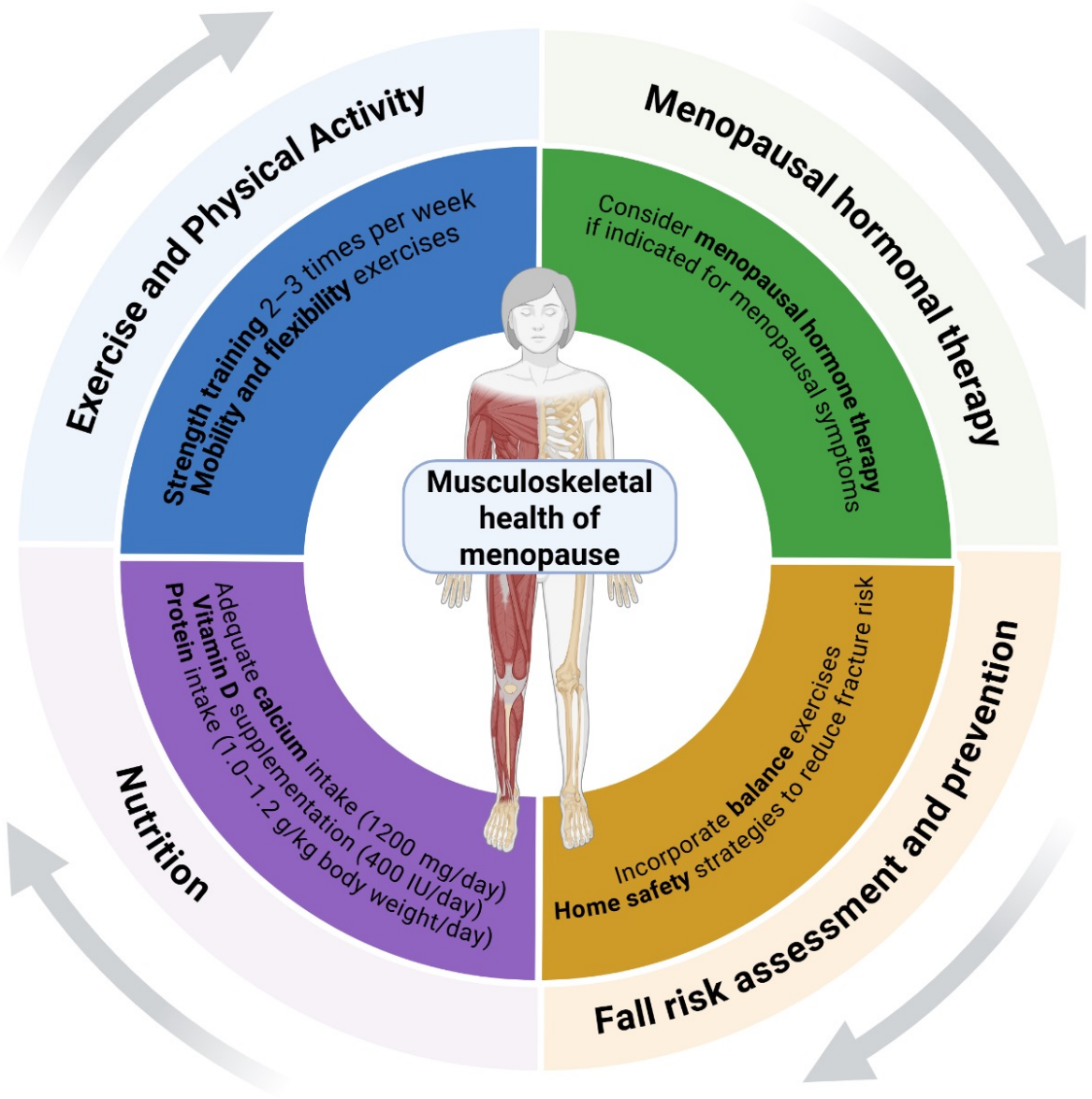

Figure 1. An integrated approach to musculoskeletal health during menopause, emphasizing the role of exercise, hormonal therapy, fall prevention, and nutrition in preserving strength, mobility, and reducing fracture risk.; *created in BioRender. Alshehri, S. (2025) https://BioRender.com/2iazucb.*

satellite cells, along with improvements in muscle strength and mobility.[33]

Conversely, other studies suggest that MHT may not be a reliable intervention for preserving muscle mass.[34] Therefore, when MHT is considered for managing other menopausal symptoms such as hot flashes or night sweating, it may be beneficial to incorporate it into a structured comprehensive plan that includes a nutritional and physical rehabilitation regimen to enhance muscle preservation and function into later life.

Conclusion

In conclusion, musculoskeletal symptoms are frequently experienced during the menopausal transition. Clinicians should address patient concerns and exclude other potential diagnoses while keeping in mind the impact of estrogen deficiency on bone, joint, and muscle health. While MHT may be beneficial in maintaining bone mass and preventing fractures, its impact on joint and muscle health remains less clear. Initiating therapy should be guided by individualized risk

assessment. Additionally, addressing modifiable risk factors, such as optimizing nutritional health and maintaining regular physical activity, can prevent further progression of musculoskeletal concerns **(Figure 1)**. Further studies are necessary to fully understand the role of MHT in musculoskeletal health.

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