CNE Article

Etiology, Assessment, and Management of Aromatase Inhibitor-Related Musculoskeletal Symptoms

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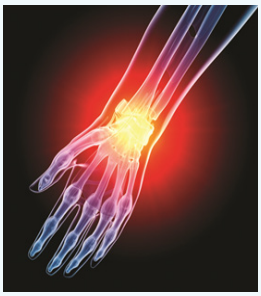

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Aromatase inhibitors (AIs) are recommended as adjuvant endocrine therapy for postmenopausal women with hormone-responsive breast cancer. With the widespread use of AI adjuvant endocrine therapy, a significant profile of musculoskeletal symptoms has emerged. Moderate to severe musculoskeletal symptoms have led some women to discontinue therapy, compromising the survival benefit. The etiology of AI-related musculoskeletal symptoms is poorly understood, which challenges development of effective management strategies. The purpose of this article is to describe AI-related musculoskeletal symptoms, review possible causes, provide assessment guidelines, and recommend management strategies based on the best available evidence. Little evidence exists for effective management strategies of AI-related musculoskeletal symptoms, and randomized clinical trials are needed to establish effective interventions. A thorough musculoskeletal assessment can help guide clinical decision making for the best individual management approach. Providers need to manage symptoms with the best available evidence to minimize symptom distress and maximize adherence to AI therapy.

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Adjuvant endocrine therapy with tamoxifen for patients with estrogen-dependent breast cancer has established benefit through significantly reduced recurrence rates and improved survival. Third generation aromatase inhibitors (AIs) (anastrozole, letrozole, and exemestane) as adjuvant endocrine therapy provide modest improvements in disease-free survival compared to tamoxifen in postmenopausal hormone-responsive breast cancer survivors (Dowsett et al., 2010; Josefsson & Leinster, 2010); however, AIs have failed to improve overall patient survival (Freedman & Winer, 2010). Despite the modest improvement in disease-free survival and similar outcomes for overall survival compared to tamoxifen, AI therapy alone for five years or given sequentially following two to three years of tamoxifen is recommended for postmenopausal women with hormone-positive breast cancer (Burstein et al., 2010). However, when the absolute benefit of one therapy versus another is small, evaluation of the safety and side-effect profile of the individual therapies is essential (Freedman & Winer, 2010).

With the widespread use of AI adjuvant endocrine therapy, a significant profile of musculoskeletal symptoms has emerged. Those symptoms are reported in 33%–50% of patients and have been associated with poor adherence, potentially leading to discontinuation of adjuvant treatment (Henry et al., 2012). However, the underlying mechanism of musculoskeletal symptoms is poorly understood and evidence is lacking to direct symptom management.

Adherence is critical in the success of therapeutic interventions, particularly with long-term treatments, such as AIs, when women are expected to take daily oral agents for at least five years. However, a significant number of patients on AI therapy discontinue their therapy because of adverse side effects (Miaskowski, Shockney, & Chlebowski, 2008). The current article will describe AI-related musculoskeletal symptoms, physiologic