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## **MOVE AGAIN IN BREAST CANCER: A Randomized Controlled Trial of Structured Exercise on Quality of Life in Premenopausal Women with Aromatase Inhibitor-Induced Arthralgia**

**Background:** Aromatase inhibitor-associated arthralgia (AIA) affects approximately 50% of breast cancer survivors, significantly impairing quality of life (QoL) and treatment adherence. While physical exercise shows promise as a non-pharmacological intervention, optimal prescription parameters remain undefined, particularly in premenopausal women undergoing aromatase inhibitor (AI) therapy with ovarian suppression.

**Purpose:** To investigate whether structured physical exercise improves health-related QoL in premenopausal breast cancer survivors experiencing AIA, and to compare different exercise modalities.

**Methods:** This single-blind randomized controlled trial will enroll 54 premenopausal women with hormone receptor-positive breast cancer receiving AI therapy with ovarian suppression and experiencing AIA. Participants will be randomized to: (1) aerobic-focused exercise, (2) resistance-focused exercise, or (3) usual care control. Both intervention groups will receive 10 weeks of supervised bi-weekly exercise sessions, while the control group will receive general exercise recommendations. Primary outcome: health-related QoL assessed by SF-36 Physical Component Summary at 3 months. Secondary outcomes include joint pain (Brief Pain Inventory, Visual Analogue Scale), physical function (handgrip strength, isokinetic dynamometry, balance, Senior Fitness Test Battery), body composition (bioelectrical impedance analysis), and comprehensive biomarker panel including inflammatory markers (hs-CRP, IL-1 $\beta$ , IL-6, TNF- $\alpha$ ), bone turnover markers ( $\beta$ -CrossLaps, osteocalcin, calcium, phosphorus), and neurotrophic and vascular factors (BDNF, VEGF, MCP-1). Assessments will be conducted in each group at baseline, 3 and 9 months.

**Expected Results:** We hypothesize that both exercise intervention groups will demonstrate significant improvements in QoL and arthralgia reduction compared to usual care. We expect favorable changes in physical function, body composition, inflammatory status, bone metabolism, and neurotrophic factors, helping to elucidate biological mechanisms underlying exercise benefits.

**Conclusions:** This study will provide evidence to define structured exercise prescriptions for managing AIA in premenopausal women, potentially improving treatment adherence and reducing cancer recurrence risk. The comprehensive biomarker assessment will enhance understanding of biological pathways through which exercise exerts therapeutic effects.

### **Keywords**

Breast cancer, Aromatase inhibitors, Arthralgia, Exercise prescription, Quality of life

### **Conflict of Interest & Ethical Approval**

yes

### **Abstract submitters declaration**

yes

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