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# Pilot study of acupuncture for the treatment of joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients

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**Abstract**
*Introduction* Aromatase inhibitors (AIs) have become the standard of care for the adjuvant treatment of postmenopausal, hormone-sensitive breast cancer. However, patients receiving AIs may experience joint symptoms, which may lead to early discontinuation of this effective therapy. We hypothesize that acupuncture is a safe and effective treatment for AI-induced arthralgias.
*Methods* Postmenopausal women with early-stage breast cancer who had self-reported musculoskeletal pain related to adjuvant AI therapy were randomized in a crossover study to receive acupuncture twice weekly for 6 weeks followed by observation or vice-versa. The intervention included full body and auricular acupuncture, and a joint-specific point prescription. Outcome measures included the Brief Pain Inventory-Short Form (BPI-SF), Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index, the Functional Assessment of Cancer Therapy-General (FACT-G) quality of life measure, and serum levels of inflammatory markers, IL-1β and TNF-α.
*Results* Twenty-one women were enrolled and two discontinued early. From baseline to the end of treatment, patients reported improvement in the mean BPI-SF worst pain scores (5.3 to 3.3, $p=0.01$), pain severity (3.7 to 2.5, $p=0.02$), and pain-related functional interference (3.1 to 1.7, $p=0.02$), as well as the WOMAC function subscale and FACT-G physical well-being ($p=0.02$ and 0.04, respectively). No adverse events were reported.
*Discussion/conclusions* In this pilot study, acupuncture reduced AI-related joint symptoms and improved functional ability and was well-tolerated.
*Implications for cancer survivors* Musculoskeletal side effects are common among breast cancer survivors on adjuvant AI therapy, therefore, effective treatments are needed for symptom relief and to improve adherence to these life-saving medications.

**Keywords** Acupuncture · Aromatase inhibitor · Breast cancer · Joint pain/stiffness

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## Introduction

Recent clinical trials have demonstrated that aromatase inhibitors (AIs) are more effective than tamoxifen at

reducing breast cancer recurrence and these have become the standard of care [1–4]. A problem with AIs is that large adjuvant trials of AIs for breast cancer treatment [1, 2, 4] indicate that 20–30% of women taking AIs experience musculoskeletal disorders including joint pain and stiffness (arthralgia). In the community, the rate of AI-related arthralgia appears to be higher. In a survey of 200 breast cancer patients on adjuvant AI therapy, over 40% of women reported worsening or new-onset joint pain or stiffness after starting AIs [5]. Among those with AI-related joint symptoms, about two-thirds experienced moderate to severe symptoms. Donnellan et al. found that up to 50% of patients on anastrozole for metastatic breast cancer experienced musculoskeletal pain and 5% discontinued treatment due to musculoskeletal symptoms [6]. This musculoskeletal pain often does not respond to conventional pain medications, may lead to noncompliance, and may reduce patients' quality of life. The mechanism of AI-related arthralgia is unknown, but may be related to estrogen deprivation [7, 8] and the release of proinflammatory cytokines, such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) [9].

Acupuncture is a popular non-pharmacological modality used for treating a variety of conditions, including musculoskeletal pain. The analgesic properties of acupuncture may be mediated by the release of opioid peptides and serotonin [10, 11]. Acupuncture has been shown to have short-term analgesic effect in musculoskeletal pain [12, 13], and clinical trials have found that patients with knee osteoarthritis have less pain when acupuncture is used as an adjunct to conventional treatments [14]. We undertook a pilot study of the efficacy and safety of acupuncture in reducing joint symptoms related to AI use.

## Materials and methods

### Participants

Women who were postmenopausal, as determined by cessation of menses for at least 1 year or FSH>20 mIU/mL, with a history of stage I, II, or IIIa hormone receptor-positive breast cancer, and currently taking a third-generation aromatase inhibitor (anastrozole, letrozole, or exemestane) for at least 6 months were eligible for this study. Included in this study were those who reported ongoing pain and/or stiffness in one or more joints, which started or worsened after initiation of AI therapy, and who had a baseline worst pain score on the Brief Pain Inventory-Short Form (BPI-SF) [15] of ≥3 points on a scale of 0 to 10. Excluded from the study were patients who had previously received acupuncture for their AI-induced joint symptoms; had received acupuncture within the six months prior to study entry; had inflammatory, metabolic, or neuropathic arthropathies, bone fracture or surgery of an afflicted extremity during the preceding 6 months; were currently taking steroids (oral or injected) or narcotics; or had severe concomitant illness or metastatic disease, severe coagulopathy or bleeding disorder, or dermatologic disease within the acupuncture area. All patients provided informed consent prior to enrollment. The Columbia University Institutional Review Board approved the study protocol prior to study commencement.

### Procedures

Patients were randomized to 30-minute acupuncture sessions twice weekly for six weeks, followed by observation for 6 weeks or to observation followed by acupuncture. During this time patients were permitted to take non-narcotic and non-steroidal pain medications as needed. Patients were asked to complete a baseline questionnaire covering demographic information (age, educational level, employment status, regular physical activity) and reproductive history (years since menopause, natural or induced menopause). Participants were also surveyed on their use of complementary and alternative medicine. At baseline, 6 weeks, and 12 weeks, history and physical examinations were performed and self-administered questionnaires including the BPI-SF, Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index Version 3.1 [16], and Functional Assessment of Cancer Therapy-General (FACT-G) [17] were completed. Follow-up assessments were conducted on the same day as the final acupuncture session. Telephone interviews were conducted every 2 weeks during the 12-week intervention to assess for adverse events and any changes in analgesic use. Serum was obtained at baseline and post-treatment.

The acupuncture protocol and procedures employed were devised with adherence to the Standards for Reporting of Controlled Trials in Acupuncture (STRICTA) recommendations that are currently followed in order to attempt to improve appraisal, interpretation, and challenges unique to acupuncture research [18]. Our acupuncture rational was selected based on a standard Traditional Chinese Medicine (TCM) point prescription to treat musculoskeletal pain and the National Acupuncture Detoxification Association (NADA) protocol applied to one ear, to relieve pain and decrease stress [19]. The protocol consisted of a standardized set of acupuncture points given twice weekly for 30 min over 6 weeks, which included full body acupuncture and auricular acupuncture in alternating ears. In addition, each session included a specific point prescription tailored to up to three of the patient's most painful areas (shoulder, wrist, fingers, lumbar area, hip or knee). Points were selected based on standard texts and informal practitioner query and expertise and were applied to standard needling depths [19]. The NADA protocol applied in one ear is based on auricular acupuncture that is rooted in a classic text of Chinese medicine (Huang

Di Nei Jing, Chapter 28), stating that "All the vessels congregate in the ear" [20]. Moreover, the practice of auricular acupuncture and the use of the NADA protocol have been demonstrated to be helpful in clinical trials for various conditions, including pain reduction [21]. An initial informal piloting of the protocol included enactment of the standardized point prescription in two healthy consenting adults who were not study participants.

Acupuncture needles were single-use, sterile, and disposable. Full body acupuncture needles were 25 mm or 40 mm and 34 gauge (Cloud & Dragon, Wujiang City Cloud & Dragon medical Device Co, Ltd, China) and auricular needles were 15 mm and 38 gauge (Seirin, Seirin-America Inc., Weymouth, MA). The needling protocol consisted of first swabbing all points with alcohol and needling auricular points, then needling full-body points. Needles were inserted to the proper needling depth as determined by standard point locations and a *de qi* sensation was obtained at all standardized full body acupuncture points. *De qi* is defined as a feeling of soreness, numbness, distention, or heaviness around the point after the needles are inserted to a certain depth; at the same time, the practitioner may feel a sense of tenseness around the needle [19]. The needles remained *in situ* for 20–25 min during which time the acupuncturist returned to stimulate the needles once, utilizing even needle technique (defined as lightly rotating the needle back and forth up to six times) in order to re-elicit the *de qi* sensation. The full body acupuncture points given at each visit included SJ 5-wai guan (alternate name TB 5), GB 41-zulin qi, GB 34-yang ling quan, LI 4-he gu, ST-41-jie xi, and KD 3-tai xi. The auricular acupuncture points needled at each visit in one ear and alternating ears with each treatment included *shen men*, kidney, liver, upper lung, and sympathetic. The joint specific point protocols for the shoulder, wrist, fingers, lumbar area, hip and knee are as follows: shoulder (LI-15, SJ-14, SI-10); wrist (SJ-4, LI-5); fingers (SI-5, SI3, ba xie, LI-3); lumbar (Du-3, Du-8, UB-23); hip (GB-30, GB-39); and knee (SP-9, SP-10, ST-34). All treatments were provided by one acupuncturist licensed in New York State.

## Measures

The BPI-SF has been used to assess the severity of pain, to evaluate the impact of pain on daily functions, and to monitor the effects of treatment in patients with cancer and other chronic illnesses [15]. This 14-item questionnaire asks patients to rate pain and the degree to which it interferes with activities on a 0 to 10 scale. Severity is measured as average pain, pain right now, worst pain, and least pain. The severity composite score was calculated as the arithemetic mean of the four severity items; the mean was calculated only when at least three of the four individual items were not missing at a given assessment. The BPI also includes a seven-item Pain Interference scale that describes how pain has interfered with: 1) general activity, 2) mood, 3) walking ability, 4) normal work, 5) relations with others, 6) sleep, and 7) enjoyment of life. The arithmetic mean of the seven interference items was calculated only when at least four of the seven individual items were not missing at a given assessment [22]. Numeric rating scales such as the BPI are among the most common, valid, and reliable measures used to assess cancer pain severity, and are preferred by patients over visual analog scale measures [23].

The WOMAC index Version 3.1 is a validated measure for assessing osteoarthritis of the knees or hips and consists of 24 questions related to three subscales: pain (0–500), stiffness (0–200), and physical function (0–1,700) [16]. The FACT-G measures four domains of quality of life, including physical, functional, social, and emotional well-being [17]. The FACT scales have five response levels ("not at all" to "very much"), where higher scores reflect better well-being and fewer symptom problems. Additional efficacy endpoints included change in dosage and frequency of analgesic use (acetaminophen, NSAIDs, or cyclooxygenase-2 inhibitors) and the frequency and severity of adverse events according to NCI Common Terminology Criteria Version 3.0 [24], as assessed by telephone interviews conducted every 2 weeks for 12 weeks.

In addition, participants were asked about their attitudes towards acupuncture at baseline and after the 6-week intervention. We asked whether acupuncture is a useful treatment for pain or relaxation, whether they would recommend it to a friend, and whether the treatments are painful or enjoyable. Participants responded using a 5-point scale (Not at all/A little bit/Moderately/Quite a bit/Extremely).

Human interleukin 1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α) in serum were determined by enzyme-linked immunosorbent assay (ELISA) using a commercially available ELISA kit (R&D Systems Inc., Minneapolis, MN). ELISA was performed according to the manufacturer's instructions. The values were converted to pg/ml by reference to a standard curve that was generated in parallel to the test samples. According to the manufacturer, the sensitivity of the assays were <0.1 pg/ml for IL-1β and <0.06 pg/ml for TNF-α.

## Statistical analysis

The primary objective was to determine the BPI-SF worst pain item (question no. 2) before and after the acupuncture intervention on a continuous scale. This was chosen as our a priori primary endpoint because it was used as a screening question to determine eligibility into the trial (BPI worst pain item ≥3 points on a scale of 0 to 10). To address this question, paired t-tests were used to compare pre- and post-treatment values for each of the outcome measures. In addition, the group randomly assigned to receive immediate

acupuncture was compared to the group assigned to receive delayed treatment. Two-sample t-tests were used to compare average change in BPI-SF scores between the two groups. A sample size of 20 has greater than 90% power to detect a reduction of 2 points or more on the BPI-SF worst pain item (question no. 2) at a 5% significance level, assuming a standard deviation of difference in score of matched pairs of 2.5 points. A reduction of 2 or more points on the BPI-SF worst pain item was categorized as a clinically meaningful decrease in pain. All statistical analyses were performed using SAS version 9.1.

## Results

Between October 2005 and March 2006, 21 patients were enrolled. Two patients discontinued treatment prematurely due to scheduling difficulties within the first 3 weeks of treatment. Baseline demographic and clinical characteristics are described in Table 1. The mean age of the women enrolled was 59 years (range 46–73). Twelve patients (57%) were white, one (5%) black, five (24%) Hispanic, and three (14%) Asian. The median time since menopause was 9 years (range, 2–31). Eleven patients (55%) had experienced natural menopause, 3 (15%) underwent surgical menopause, and six patients (30%) reported chemotherapy-induced menopause. The median pain score at baseline, as measured by the BPI-SF (worst pain), was 5 (range 3–10). At baseline, 32% reported mild joint pain (BPI worst pain of 3–4), 58% moderate pain (5–7), and 10% severe pain (8–10). At study entry, only one patient reported having used acupuncture previously. However, most other patients reported using other complementary therapies (Table 2).

From baseline to the end of treatment, patients reported improvements in joint pain and stiffness, and quality of life (Table 3). Sixty percent reported at least a 2-point improvement in the BPI-SF worst pain score and 13% had worsening of symptoms. The mean BPI-SF worst pain scores declined (5.3 to 3.3, $p=0.01$), as did scores for pain severity (3.7 to 2.5, $p=0.02$), and pain-related interference (3.1 to 1.7, $p=0.02$). The total (normalized) WOMAC score (80.9 to 47.4, $p=0.04$) and the function subscale (454.0 to 288.8, $p=0.02$) also improved. Measures of pain (113.5 to 78.8, $p=0.15$) and stiffness (63.0 to 29.4, $p=0.07$) also improved, but the changes did not attain statistical significance. Physical well-being measured by the FACT-G showed a significant improvement directly following the last treatment (19.9 to 23.4, $p=0.03$).

Patients in the immediate acupuncture group reported improvements in joint pain and stiffness, physical function, and quality of life compared to the delayed acupuncture group (Fig. 1). These improvements did not persist 6 weeks after they completed acupuncture treatment. In the delayed treatment group, symptoms worsened prior to initiating acupuncture, and then improved following treatment. Differences in scores between the treatment group (immediate acupuncture) and controls (delayed acupuncture) were not statistically significant.

Of 11 patients (52%) who reported taking analgesics (acetaminophen, NSAIDs, or COX-2 inhibitors) at baseline, nine (82%) reported decreasing or discontinuing analgesics after 6 weeks of acupuncture. In the post-treatment

**Table 1** Baseline demographic and clinical characteristics

| Clinical characteristic | Frequency |
|---|---|
| *N* | 21 |
| Median age, years (range) | 59 (46–73) |
| Race, no. (%) | |
| White | 12 (57) |
| Black | 1 (5) |
| Hispanic | 5 (24) |
| Asian | 3 (14) |
| Employment, no. (%) | |
| Full-time | 9 (45) |
| Part-time | 3 (15) |
| Retired | 6 (30) |
| Disabled | 2 (10) |
| Menopause, no. (%) | |
| Natural | 11 (55) |
| Surgical | 3 (15) |
| Chemotherapy-induced | 6 (30) |
| Median years since menopause (range) | 9 (2–31) |
| Median body mass index, kg/m$^2$ (range) | 28 (19–44) |
| Aromatase inhibitor therapy, no. (%) | |
| Anastrozole | 14 (67) |
| Letrozole | 4 (19) |
| Exemestane | 3 (14) |
| Stage of breast cancer, no. (%) | |
| I | 10 (48) |
| II | 10 (48) |
| III | 1 (4) |

**Table 2** Use of CAM practitioners and therapies (*N*=21)

| CAM | *N* (%) |
|---|---|
| Practitioners | |
| Chiropractor | 9 (43) |
| Massage practitioner | 8 (38) |
| Acupuncturist | 1 (5) |
| Herbalist | 1 (5) |
| Spiritual healer | 1 (5) |
| Therapies | |
| Vitamins | 15 (71) |
| Nutritional supplements | 6 (29) |
| Glucosamine/chondroitin | 9 (43) |
| Herbal pills, tinctures, or medicinal teas | 7 (33) |

**Table 3** Change in pain, stiffness and quality of life following 6 weeks of acupuncture therapy

| | Baseline mean (SD) | After aacupuncture Mean (SD) | *P*-value |
|---|---|---|---|
| BPI | | | |
| Worst pain no. 2 (0–10) | 5.3 (2.3) | 3.3 (2.3) | 0.008 |
| Pain severity (0–10) | 3.7 (2.3) | 2.5 (1.9) | 0.022 |
| Pain-related interference (0–10) | 3.1 (1.8) | 1.7 (1.8) | 0.015 |
| WOMAC | | | |
| Pain (0–500) | 113.5 (106.0) | 78.8 (85.3) | 0.145 |
| Stiffness (0–200) | 63.0 (60.8) | 29.4 (41.2) | 0.067 |
| Function (0–1,700) | 454.0 (328.5) | 288.8 (295.6) | 0.019 |
| Normalized (0–300) | 80.9 (62.4) | 47.4 (52.5) | 0.040 |
| FACT-G | | | |
| Physical well-being (0–28) | 19.9 (5.8) | 23.4 (3.8) | 0.030 |
| Social/family well-being (0–24) | 20.1 (6.1) | 20.8 (5.5) | 0.127 |
| Emotional well-being (0–28) | 19.6 (4.0) | 20.8 (2.8) | 0.606 |
| Functional well-being (0–28) | 20.5 (5.3) | 22.1 (4.3) | 0.165 |
| Inflammatory biomarkers | | | |
| TNF-α (pg/ml) | 1.50 (1.16) | 11.87 (28.69) | 0.163 |
| IL-1β (pg/ml) | 0.142 (0.029) | 0.207 (0.104) | 0.150 |

questionnaire, 64% said that they experienced at least moderate pain relief, 71% reported at least moderate reduction in their stress level, and 73% said they would recommend acupuncture to a friend. Only 13% of patients rated acupuncture as very painful. No other toxicities referable to acupuncture were observed.

In an exploratory analysis of proinflammatory cytokines (Table 2), the mean pre- and post-treatment TNF-α scores were 1.50 pg/ml and 11.87 pg/ml, respectively (normal range 0–4.71 pg/ml). IL-1β pre- and post-treatment values were 0.142 pg/ml and 0.207 pg/ml, respectively (normal range 0–1.996 pg/ml). These differences did not reach statistical significance.

## Discussion

In this pilot study, patients reported that acupuncture relieved their AI-related joint symptoms, reduced the severity of their symptoms, and improved their functional ability. In addition, no adverse outcomes were reported, many patients reported that acupuncture was effective, relaxing and they would recommend it to others.

Aromatase inhibitor therapy has become the standard of care for postmenopausal women with both early- and late-stage hormone-sensitive breast cancer [1–4, 25]. The success of AIs as adjuvant treatment depends, however, on patients' ability and willingness to adhere to long-term treatment. Surprisingly, studies show that despite the known benefits of tamoxifen, 23–40% of women discontinue therapy early [4, 26]. Although AIs are considered to have a better side-effect profile than tamoxifen, significant musculoskeletal discomfort may lead to decreased quality of life, suboptimal adherence, and possibly reduced efficacy. Our study suggests that acupuncture may be an effective therapy to reduce the musculoskeletal side effects associated with AI treatment.

The exact mechanism of AI-related arthralgia is unclear, but may be related to estrogen deprivation. Several clinical and preclinical studies support the role of estrogen in osteoarthritis, which is characterized by progressive articular cartilage degeneration. The development of AI-induced musculoskeletal disorders may be analogous to the development of hand and knee osteoarthritis at menopause [27]. Observational studies of the incidence and prevalence of osteoarthritis in postmenopausal women with and without hormone replacement therapy have provided strong support for a protective effect of estrogens against osteoarthritis [28–30]. In addition, in the Women's Health Initiative, postmenopausal women who took estrogen reported less joint pain or swelling than those who did not take estrogen [31]. We recently reported that being overweight and prior tamoxifen therapy were inversely associated with AI-related joint symptoms [5]. However, the strongest predictor of AI-induced joint pain and stiffness was prior exposure to taxane chemotherapy [5].

Various animal and *in vitro* studies suggest that estrogen may play a role in the regulation of cartilage turnover and development of joint disease. In ovariectomized rats, estrogen prevented the cartilage breakdown caused by IL-1β, a proinflammatory cytokine that plays a critical role in the pathogenesis of OA [32]. Decreased estrogen results in increased release of proinflammatory cytokines, such as IL-1β and TNF-α, from monocytes and macrophages [9]. These cytokines promote cartilage reabsorption, inhibit synthesis of proteoglycans and cause inflammation [9,

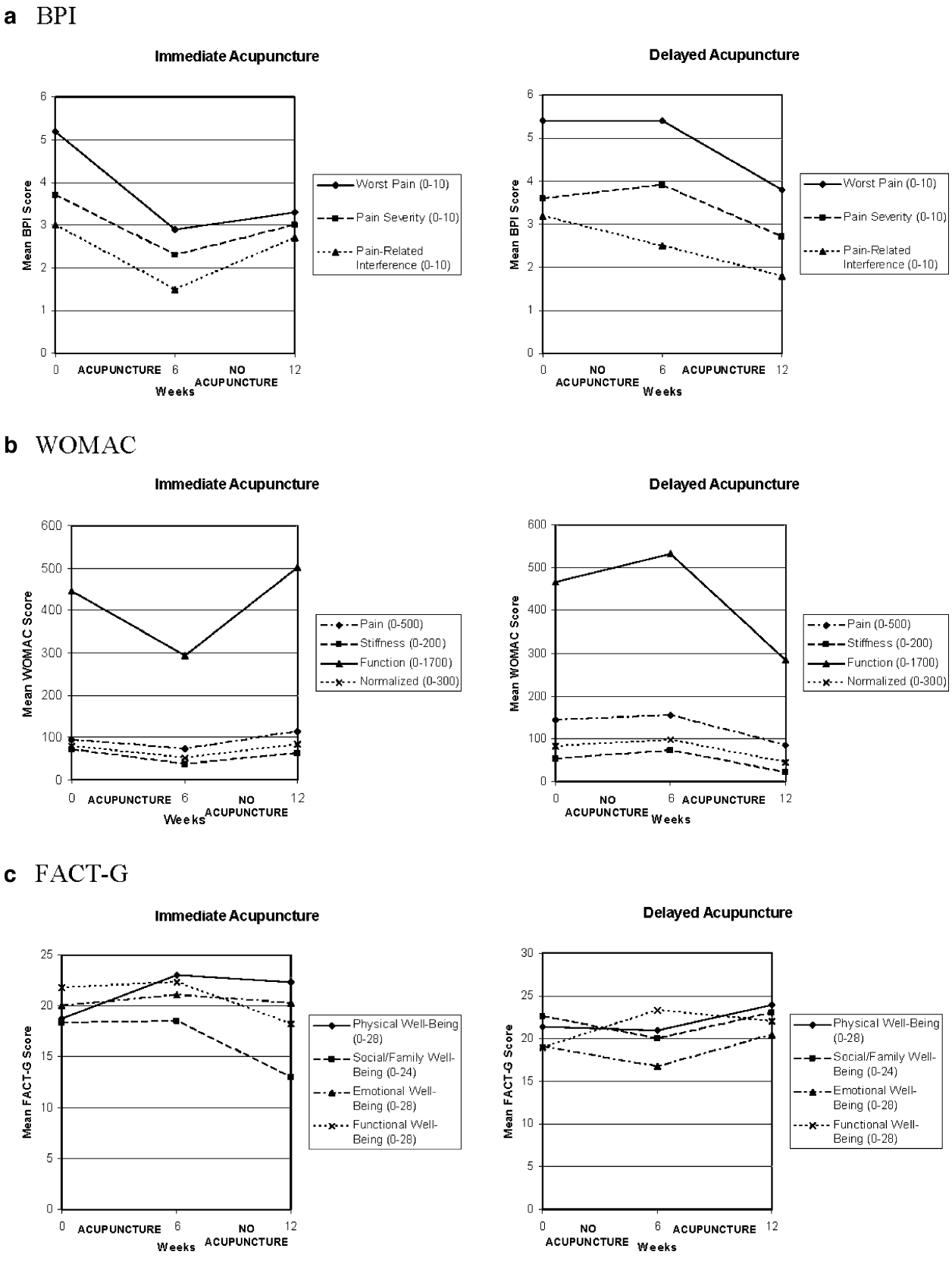


**Figure 1** Joint pain, stiffness, and quality of life measures for the immediate and delayed acupuncture groups: **a** Mean BPI scores for immediate and delayed acupuncture groups, **b** Mean WOMAC scores for immediate and delayed acupuncture groups, **c** Mean FACT-G scores for immediate and delayed acupuncture groups.

33–35]. In the assessment of laboratory biomarkers for this study, neither TNF-α nor IL-1β levels corresponded with therapeutic response during the course of acupuncture treatment. Additional study in this area is warranted to clarify whether those biomarkers have any association with AI-induced joint pain.

Ideally, symptom relief from AI-related arthralgia should be through non-hormonal mechanisms, so as not to interfere with the therapeutic effect of the drug. The exact mechanisms of the analgesic effects of acupuncture are unclear. Endogenous opioid peptides are considered major candidates for the role of acupuncture in the central nervous system. Studies have demonstrated that acupuncture causes an increase in opioid peptides in the plasma and cerebrospinal fluid in humans [36] and is antagonized by the opioid receptor antagonist, naloxone [37]. Others have postulated that polymodal receptors (PMRs) may play an important role in the peripheral mechanisms of acupuncture action [38]. Discharges of PMRs in deep tissue correlate with the intensity of *de qi* sensation of acupuncture [39]. Improvement in blood flow has been an additional proposed mechanism of acupuncture with reports of increased local and remote muscle blood flow in humans after acupuncture [40, 41].

Our report contributes to a growing body of evidence that acupuncture may have a role in the supportive care of cancer patients and survivors; previous data suggest that acupuncture is effective in reducing chemotherapy-induced nausea and vomiting [42], xerostomia [43–45], leukopenia [46], and other chemoradiotherapy-induced symptoms [47].

With regard to cancer pain, Hui et al. [48] suggest, there may be a need distinguish between different types of cancer-related pain in the design of acupuncture studies, since musculoskeletal pain appears to be more responsive to acupuncture therapy, than other types of pain. Benefits of acupuncture have also been reported for the treatment of cancer-related neuropathic pain [49]. In addition, location of acupuncture may have a strong impact on the ability to detect an effect, as one well-designed randomized controlled trial of auricular acupuncture for cancer pain showed statistically significant pain relief in comparison with placebo ear acupuncture [49]. While one recent systematic review found no evidence that acupuncture is of benefit for overall cancer-related pain, [50] most of the studies included in the meta-analysis were non-blinded or uncontrolled clinical trials, which were limited by small samples sizes and methodological flaws.

There are several reports that acupuncture has analgesic efficacy in the treatment of non-cancer related musculoskeletal pain [51]. Randomized trials have concluded that acupuncture is more effective than sham (placebo) acupuncture in the treatment of knee and back pain [52], and that acupuncture appears to be effective in the treatment of osteoarthritis of the knee [52, 53]. Our results support substantial prior evidence that acupuncture is a safe and generally well-tolerated procedure [54, 55].

The use of complementary and alternative medicine (CAM) is growing in the United States, and breast cancer patients are more likely than those with other cancers to use CAM therapies in conjunction with conventional treatment modalities [56–58]. Acupuncture has increased in popularity and acceptance in the United States in recent decades, and is now regulated by the U.S. Food and Drug Administration as a standard medical device. The use of acupuncture and other alternative techniques is expected to continue to increase.

While guidelines including the STRICTA recommendations have been adopted and applied to acupuncture research, there is still no consensus on the best way to conduct controlled studies of acupuncture. We implemented a randomized cross-over design with a delayed acupuncture arm serving as the control group. We found that certain measures got worse in the delayed acupuncture group prior to starting acupuncture. This may be due to the natural history of the AI-related joint syndrome or the subjective nature of these measures and the anticipation of starting acupuncture. In the immediate acupuncture group, initial improvements in pain scores did not persist six weeks after they completed acupuncture treatment. Similarly, other acupuncture studies which have implemented a cross-over design did not find evidence of carryover effects of acupuncture [59–61]. However, the sample sizes were small and the follow-up was short, and it would be premature to speculate about the long-term effects of acupuncture, since most studies do not assess patients following the intervention.

Limitations of our study include the small sample size and the lack of blinding to the acupuncture intervention. Randomized, controlled studies of acupuncture protocols often utilize sham acupuncture as the control group. Sham acupuncture can use either false points or non-penetrating fake needles, but either method may confer benefits. These benefits may be due to a physiologic effect of needling even when not performed according to established principles or to differences in intensity of provider contact [62]. Future study designs will need to account for this in protocol development and analysis.

To our knowledge, this report is the first to describe the use of acupuncture or any other intervention to treat AI-related joint symptoms. With the increasing use of long-term aromatase inhibitor therapy in the adjuvant setting, AI-induced arthralgia is becoming a major issue for breast cancer survivors. Significant musculoskeletal discomfort may lead to suboptimal adherence, and possibly reduced efficacy. Therefore, interventions are needed to manage this treatment-related side effect and improve overall quality of life among breast cancer survivors. Our study suggests that acupuncture is a promising non-pharmacological modality

for relieving AI-related joint pain and stiffness. These findings are encouraging and need to be confirmed in a larger randomized controlled study.

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