Original Research

Ageing perceptions and non-adherence to aromatase inhibitors among breast cancer survivors

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Abstract *Purpose:* Aromatase inhibitors (AIs) are a potentially life-saving treatment for breast cancer survivors, yet poor adherence to treatment is a prevalent problem. A common adverse effect of AI treatment is arthralgia, which is identified by survivors as a major reason for treatment discontinuation. Women who experience arthralgia on AIs often report feeling they have aged rapidly while on the treatment. In the present study, we examined whether arthralgia-associated ageing perceptions predicted non-adherence.

Patients and methods: We conducted a prospective cohort study among women with stage I—III breast cancer, who were on an AI and completed the Penn Arthralgia Aging Scale within 2 years of AI initiation. Adherence data were abstracted from medical charts by trained raters. Cox proportional hazard analysis was used to determine the relationship between ageing perceptions and time to non-adherence. All analyses included adjustments for joint pain severity.

Results: Among 509 participants, 144 (28.3%) were non-adherent. As hypothesised, women with high levels of ageing perceptions were at greater risk of non-adherence than women with low levels of ageing perceptions (adjusted hazard ratio [HR], 1.71; 95% confidence interval [CI], 1.10—2.67; $p = .02$). High levels of depressive symptoms were also uniquely associated with increased risk of non-adherence (adjusted HR, 1.63; 95% CI, 1.03—2.59; $p = .04$).

Conclusion: Perceptions of ageing related to arthralgia and depressive symptoms predicted non-adherence to AIs. These findings suggest that interventions that address negative beliefs about ageing due to AI-related arthralgia and depressive mood can potentially improve rates of adherence to AIs.
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1. Arthralgia, ageing perceptions, and risk of medication non-adherence among breast cancer survivors

Breast cancer is the second deadliest cancer among women [1]. Though treatments for early-stage breast cancer are effective, cancer recurrence remains a looming concern for many patients. Aromatase inhibitors (AIs), a form of adjuvant hormonal therapy for post-menopausal patients with hormone receptor—positive tumours, help to decrease the risk of cancer recurrence and thereby decrease mortality rates [2,3]. Unfortunately, non-adherence to AIs is a prevalent problem [4—8] and leads to poor disease outcomes [9]. Many women identify joint pain, a common side-effect of AIs [10], as the reason they prematurely discontinue their treatment [6,11]. In a cohort study, joint pain severity was found to be a significant predictor of non-adherence risk such that women who scored above a predefined threshold of pain severity were more than twice as likely to prematurely discontinue their AI [12,13].

Despite the strong relationship between joint pain and adherence, not all women with high levels of arthralgia stop taking their AI. Understanding psychological responses to arthralgia may shed light on who is most at risk of non-adherence. Pain often triggers complex cognitive responses that independently contribute to physical and psychological impairment. For example, anticipation of pain and pain catastrophising explain variance in individuals' activity levels, even after pain severity is accounted for [14—16].

For women on AIs, joint pain has been found to trigger negative thoughts about ageing. Qualitative investigations and case studies have shown that women on AIs who experience joint pain tend to feel that they are ageing faster than they should be and that time is passing them by [17—19]. In prior cross-sectional work, we have found that among AI patients, arthralgia-associated ageing perceptions explain variance in depression, anxiety and the degree to which pain interferes with daily functioning, over and above pain severity [20]. In longitudinal analyses of non-cancer populations, negative ageing perceptions have been associated with lower life satisfaction, worse objective physical functioning and higher mortality risk, even after adjustments are made for health status [21—26]. Ageing perceptions have also been linked to self-reported preventative health behaviours, such as diet and exercise [23]. Overall, negative ageing perceptions have been shown to have considerable impact on a person's psychological and physical well-being, as well as on self-care behaviours.

We hypothesised that breast cancer survivors who had heightened perceptions of arthralgia-associated ageing would be at a greater risk of non-adherence to their AIs. Identifying a psychological process that leads to non-adherence can inform the development of more targeted interventions to improve AI adherence.

2. Method

We conducted a prospective cohort study among postmenopausal breast cancer survivors as part of the Wellness after Breast Cancer (WABC) study. Inclusion criteria were the following: (1) female sex, (2) aged ≥18, (3) postmenopausal status, (4) diagnosed with stage I—III hormone receptor—positive breast cancer, (5) prescribed a third-generation AI, (6) completed all primary cancer treatments (radiotherapy, chemotherapy and/or surgery) at least one month before the survey date and (7) fluent in English. Research assistants recruited cancer survivors at various stages in their AI treatment. Participants completed a survey in the breast cancer clinic after providing informed consent. The study was approved by the Institutional Review Board of the University of Pennsylvania.

We specifically focused our analysis on participants who had completed the baseline survey not more than 2 years after AI initiation. Given that arthralgia symptoms tend to emerge early in AI treatment [27], cognitive appraisals of ageing due to arthralgia would also likely develop near the beginning of the treatment course. A total of 862 breast cancer survivors were enrolled in the cohort study. Of these, one withdrew from the study, 11 did not complete the survey and seven did not have enough information in their charts to discern any adherence behaviours. To create a more homogenous sample, we excluded another 10 participants from the analysis because they were prescribed less than 5 years of AI treatment (5 years is the treatment length recommended by the American Society of Clinical Oncology [28]). Of the remaining 833 participants, 509 were currently on an AI at the time of the survey and had initiated their AI treatment less than 2 years prior, thus meeting inclusion criteria.

2.1. Measures

2.1.1. Non-adherence

Adherence outcome data were abstracted from participants' medical charts with the most recent abstractions occurring in January of 2016. Non-adherence was defined as a treatment interruption (any time off from an AI during the prescribed treatment period) and/or premature discontinuation (stopping the AI entirely before the prescribed treatment end date). These two types of non-adherence were combined to achieve greater statistical power because both have been found to predict risk of recurrence [9].

Trained coders abstracted adherence information from appointment and telephone-call notes in participants' medical charts. On average, participants were observed for 18 months post-survey. Before abstracting