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# Diet Quality, Inflammation, and Quality of Life in Breast Cancer Survivors: A Cross-Sectional Analysis of Pilot Study Data

Tonya S. Orchard, PhD, RD; Rebecca R. Andridge, PhD; Lisa D. Yee, MD; Maryam B. Lustberg, MD, MPH

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**ABSTRACT**

**Background** Modifiable lifestyle factors, such as diet quality, could reduce inflammation and improve quality of life (QOL) in breast cancer survivors, but data are inconclusive.

**Objective** To determine whether diet quality, as measured by Healthy Eating Index-2010 (HEI-2010) score, is associated with inflammation, health status, or functional outcomes affecting QOL in survivors of early-stage breast cancer.

**Design** This is a cross-sectional, secondary analysis of baseline data collected from breast cancer survivors after completion of primary therapy and before random assignment to a pilot nutritional intervention aimed at reducing side effects of aromatase inhibitor treatment.

**Participants/setting** Participants were 44 postmenopausal women with stage I to III endocrine receptor−positive breast cancer receiving outpatient care at a midwestern cancer center between November 2011 and October 2013.

**Main outcome measures** Primary outcomes were serum proinflammatory cytokines (interleukin-6 [IL-6], IL-17, and tumor necrosis factor-$\alpha$ receptor 2 [TNFR-2]). Secondary outcomes included QOL measured by the Stanford Health and Disability Questionnaire and the Functional Assessment of Cancer Therapy−Breast with Endocrine Subscale.

**Statistical analyses performed** Pearson correlation coefficients ($r$) and linear regression models were used to evaluate the relationship of dietary variables with inflammatory cytokines and QOL measures.

**Results** A higher overall HEI-2010 score (healthier diet) was associated with lower IL-6 ($r=-0.46$; $P=0.002$) and TNFR-2 ($r=-0.41$; $P=0.006$); however, associations were attenuated by body mass index (BMI) (IL=6 [$r=-0.26$; $P=0.10$]; TNFR-2 [$r=-0.30$; $P=0.06$]). In women with prior chemotherapy, a higher HEI-2010 score was strongly associated with lower IL-6 ($r=-0.67$; $P=0.009$) and TNFR-2 ($r=-0.59$; $P=0.03$) after BMI adjustment. There were no significant correlations between HEI-2010 score and QOL measures after adjustment for BMI.

**Conclusions** These data suggest the need for more rigorous investigation into the relationship of diet quality, BMI, and inflammation in breast cancer survivors.

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BREAST CANCER IS THE MOST COMMON CANCER among women in the United States with the exception of skin cancer; nearly 3.1 million women in the United States are currently breast cancer survivors.[1] As the prognosis for women diagnosed with early-stage breast cancer continues to improve, patients and clinicians are shifting their focus from survival alone to improving quality of life (QOL) and patient-centered functional outcomes.[2] Chronic inflammation has been associated with fatigue[3] and multiple other conditions affecting QOL in survivors of early-stage breast cancer, including poorer physical functioning and less vitality.[4] Pretreatment inflammatory status may predict the development of common musculoskeletal side effects, which reduce QOL and may affect treatment adherence, in postmenopausal breast cancer survivors beginning commonly prescribed adjuvant cancer treatment with aromatase inhibitors (AIs).[5] Furthermore, higher levels of the inflammatory cytokine interleukin-6 (IL-6) have been associated with negative cognitive side effects of chemotherapy in breast cancer survivors.[6] Most importantly, a lower level of inflammation is associated with improved survival in women diagnosed with early-stage breast cancer,[7,8] potentially by promoting a less favorable microenvironment for tumor growth and metastasis.[9] Thus, identification of modifiable lifestyle factors, such as diet quality or specific dietary components, which can be targeted to reduce chronic inflammation, may be an important approach to improving QOL and survival in patients with breast cancer.

Overall diet quality (ie, a healthier diet pattern) has been associated with less inflammation in various cohorts,[10,11] but

results are inconsistent.[12] One study of patients with new diagnoses of head and neck cancer revealed associations between better diet quality and lower levels of the inflammatory cytokines IL-6 and tumor necrosis factor-$\alpha$ (TNF-$\alpha$).[13] Research on diet quality and inflammation in breast cancer survivors is sparse, but results of one large cross-sectional study suggest that better diet quality is associated with lower levels of some inflammatory markers, such as C-reactive protein (CRP), but not others.[14]

The relationship between diet quality and QOL in cancer survivors is ambiguous. For example, Wayne and colleagues[15] found a direct positive association between diet quality and QOL in breast cancer survivors; however, results of recent research are less clear and seem to suggest that improving diet quality after individuals have completed primary cancer treatment, as opposed to during treatment, might be most effective in improving QOL.[16] It is not known whether diet quality after primary cancer treatment influences response to commonly prescribed adjuvant endocrine treatment such as AIs or the development of common musculoskeletal side effects related to this treatment. A preliminary step in addressing this question is determining the relationship of diet quality to inflammation and QOL measures in breast cancer survivors beginning AI treatment.

The primary objective of this research was to determine whether overall diet quality, as measured by the Healthy Eating Index-2010 (HEI-2010), is associated with systemic inflammation in postmenopausal women diagnosed with early-stage breast cancer who had completed primary cancer treatment and were scheduled to begin adjuvant endocrine treatment with AIs. The secondary objective was to determine whether diet quality is associated with health/disability status and functional outcomes important to QOL. The authors hypothesized that women who had better diet quality (ie, higher HEI-2010 scores) would have lower levels of inflammatory markers (IL-6, IL-17, and TNF-$\alpha$ receptor 2 [TNFR-2]), better health status (ie, less disability), and better functional capacity.

## METHODS

### Study Design and Participants

This is a cross-sectional secondary analysis of baseline data from 44 postmenopausal women with stage I to III hormone receptor–positive breast cancer who were within 2 weeks of initiating first-line adjuvant endocrine treatment with Food and Drug Administration–approved third-generation AIs (letrozole, anastrozole, or exemestane). Participants were enrolled in a pilot study testing effectiveness of a 6-month intervention of n-3 fatty acid supplementation versus placebo for joint symptoms, a common side effect of AI treatment.[17] The study was carried out at the Ohio State University Comprehensive Cancer Center (Clinical Trial #NCT01478477). Potentially eligible patients were recruited by physicians and the study coordinator during regularly scheduled clinic visits between November 2011 and October 2013. Exclusion criteria were concurrent malignancy; rheumatoid arthritis and other types of autoimmune and inflammatory joint disease (except fibromyalgia and osteoarthritis); known bleeding disorders; history of diabetes mellitus, heart disease, or stroke; uncontrolled current illness; and current daily use of anticoagulants or full-dose aspirin (>325 mg/day), nonsteroidal anti-inflammatory drugs, steroids, or n-3 fatty acid supplements >360 mg/day within 6 months of study initiation. A total of 277 women were assessed for eligibility; 146 did not meet eligibility criteria, and 87 were unable to participate or uninterested in participation, leaving a final sample size of 44 women for this baseline analysis. Data for this analysis were collected before random assignment to the supplement intervention or placebo group and within 2 weeks of initiation of treatment with an AI. The Ohio State University Institutional Review Board approved the study protocol, and all participants provided written informed consent.

### Dietary Assessment and HEI-2010

At the baseline study visit, women completed a food frequency questionnaire (FFQ), which was subsequently used to estimate nutrient intake and calculate HEI-2010 scores. The General Nutrition Assessment (GNA) FFQ was developed by the Nutrition Assessment Shared Resource of Fred Hutchinson Cancer Research Center (Seattle, WA) based on a previously validated FFQ used in the Women's Health Initiative (WHI).[18] The GNA and its parent WHI FFQ have the same format and analysis algorithms with minor differences in specific items; however, unlike the WHI FFQ, the GNA nutrient database continues to be updated regularly as new nutrients and food components are added to the Nutrition Data Systems for Research (NDSR). In the present study, the GNA FFQ was used to assess usual diet intake over the previous 3 months. The FFQ contained 122 questions on foods or food groups; 19 adjustment questions designed to allow more precise analysis of fat intake; and four summary questions regarding usual intake of fat, fruits, and vegetables. The Fred Hutchinson Cancer Research Center analyzed the FFQ data using the NDSR, version 2013, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis.[19] Briefly, component food items from the FFQ were linked to food items from the MyPyramid Equivalents Database[20] to estimate the food group equivalents for each line item on the FFQ. These food group equivalents, along with a few data items output by NDSR (eg, alcohol, sodium, overall calorie intake, and ratio of poly- and monounsaturated fatty acids to saturated fatty acids) were used to calculate the HEI-2010 scores.

The HEI-2010 is a scoring metric that measures diet quality in relation to conformity to the 2010 Dietary Guidelines for Americans[21] and has been used to examine relationships between diet and health-related outcomes.[22] The HEI-2010 was developed jointly by the National Cancer Institute and the US Department of Agriculture and is made up of 12 dietary components: nine adequacy components and three moderation components. A higher score (100 is maximal) corresponds to a higher-quality diet; a higher score is given for increasing consumption of "adequacy" components, and a lower score is given for increasing consumption of "moderation" components. Scoring standards for each component of the HEI-2010 are adjusted for energy intake (eg, per 1,000 kcal or as a percentage of total energy intake), except for the fatty acid component score, which is a ratio of unsaturated to saturated fatty acids.[22]

### Anthropometry

Height and weight of study participants (wearing light clothing and no shoes) were obtained by trained staff at the