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# Within-person changes in cancer-related distress predict breast cancer survivors' inflammation across treatment

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## Abstract

**Background:** Among breast cancer survivors, elevated inflammation has been linked to greater recurrence risk. Psychological processes, such as cancer-related distress, can pose threats to a survivor's longevity and wellbeing. Although distress can heighten inflammation, little is known about how fluctuations in distress during and after treatment impact a woman's own inflammation – the primary question of this study.

**Methods:** Breast cancer survivors ($n$ = 165, stages 0-III) completed a baseline visit before treatment and two follow-up visits 6 and 18 months after. At each visit, women completed the Impact of Events Scale to assess cancer-related distress, and a blood sample was collected to measure proinflammatory cytokines IL-6, TNF-α, IL-1β, and IL-8. This longitudinal study related fluctuations in survivor's own cancer-related distress (i.e., within-person effects), as well as average effects of cancer-related distress between survivors (i.e., between-person effects) to inflammatory changes across visits.

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**Results:** Women had elevated inflammation at visits where they expressed more cancer-related distress than what was typical. In contrast, the average cancer-related distress was not associated with inflammation.

**Conclusion:** Larger increases in a women's cancer-related distress was linked with higher inflammation across visits. Comparing a survivor's own cancer-related distress to her average levels may prove useful in identifying links between distress and inflammation.

### Keywords

cancer survivors; inflammation; cancer-related distress; avoidance; intrusive thoughts

## 1. Introduction

Chronic inflammation in adults without a cancer diagnosis increases morbidity and disability (Ferrucci et al., 2002; Liu et al., 2017). A proinflammatory environment promotes tumor initiation, growth, and metastases, contributing to poorer prognoses, risk for recurrence, and reduced survival among cancer patients (Aggarwal, Shishodia, Sandur, Pandey, & Sethi, 2006; Smyth, Cretney, Kershaw, & Hayakawa, 2004; Thaker et al., 2006). Inflammation also contributes to distressing physical side effects associated with cancer treatment and survivorship, including fatigue and pain (Fagundes, LeRoy, & Karuga, 2015). Further, heightened inflammation increases the risks of comorbid disease development including cardiovascular disease, osteoporosis, diabetes, and others among cancer survivors (Alfano et al., 2017; Pierce et al., 2009; Smyth et al., 2004). These conditions pose additional threats to survivors' long-term health and physical functioning.

The stressors that survivors experience promote immune dysregulation and reduce quality of life among survivors (Avis et al., 2020; Powell, Tarr, & Sheridan, 2013; Shrout et al., 2020). Both acute and chronic stress increase inflammation (Marsland, Walsh, Lockwood, & John-Henderson, 2017; Rohleder, 2019). Many stressors emerge throughout the cancer trajectory including diagnosis, treatment, physical side effects, medical decision-making, and changes in role functioning. When people experience a variety of or prolonged stressors, distress is a typical result. Cancer-related distress can prime physiological dysfunction and high symptom burden among breast cancer survivors. Although the majority of available data on cancer-related distress focuses on differences between survivors, within-person changes (e.g., how a woman's distress varies compared to what is typical for her) may provide a new window into inflammatory changes among breast cancer patients (Thornton & Andersen, 2006). The physical symptoms and side effects commonly associated with treatment provoke cancer-related distress (Jim, Andrykowski, Munster, & Jacobsen, 2007). Although typically highest within the first year following cancer diagnosis, cancer-related distress can remain elevated following treatment, impacting physical and psychological well-being (Bleiker, Pouwer, Van Der Ploeg, Leer, & Ader, 2000; Buzaglo et al., 2016).

Burdensome components of cancer-related distress can include intrusive negative thoughts and cognitive and emotional avoidance. Intrusive thoughts in response to a stressor such as a cancer diagnosis and/or treatment typically include unwanted thoughts, images, and dreams (Primo et al., 2000). Survivors may also avoid particularly unpleasant or overwhelming

thoughts and emotions associated with their cancer diagnosis and treatment (Primo et al., 2000). Avoidance poses numerous threats to survivors physical and psychological wellbeing, including heightened depressive and anxiety symptoms and increased pain and fatigue (Aguirre-Camacho et al., 2017; Bauer et al., 2016). Intrusive thoughts also heighten physical symptoms associated with breast cancer treatment including pain, sleep problems, and fatigue (Dupont, Bower, Stanton, & Ganz, 2014). These negative and unwanted thoughts also inhibit psychological adjustment following cancer treatment (Cordova et al., 1995; Lewis et al., 2001; Matsuoka et al., 2002). Overall, compared to newly diagnosed breast cancer patients who did not avoid or experience negative intrusive thoughts, those who experienced higher rates of intrusion and avoidance had higher levels of anxiety and depressive symptoms throughout treatment (Donovan-Kicken & Caughlin, 2011; Primo et al., 2000). Rumination, one form of intrusive thoughts, is associated with higher c-reactive protein (CRP) in healthy women (Zoccola, Figueroa, Rabideau, Woody, & Benencia, 2014). To date, no research has tested how intrusive thoughts and avoidance may relate longitudinally to inflammation among healthy participants or breast cancer survivors.

Heightened cancer-related distress can impair survivors' physical functioning and quality of life. However, it is unknown whether deviations in a woman's own cancer-related distress or her distress compared to others contributes to higher inflammation. This study used a novel approach to examine associations between cancer-related distress and inflammation among survivors across three in-person laboratory visits. We assessed how within-person increases in cancer-related distress, as well as how average distress levels, related to fluctuations in inflammation across visits. Testing within-person processes are important in understanding how a survivor's own distress changes before and after treatment in addition to how these changes relate to inflammation across visits, rather than how distress and inflammation compare to other women. Thus, examining effects both between and within survivors offers provides insight into how distress impacts inflammation as well as how changes in distress are associated with changes in inflammation from visit to visit within a given survivor. At the between-person level, we expected that higher average cancer-related distress would be associated with higher average inflammation. Within-person increases in cancer-related distress were hypothesized to accompany higher inflammation. We examined how the two aspects of cancer-related distress—intrusive thoughts and avoidance—independently related to inflammation across study visits. We expected that greater increases in intrusion and avoidance, as well as higher average intrusion and avoidance, would independently predict higher inflammation. Lastly, to assess bidirectionality between inflammation and cancer-related distress, we tested alternative models to determine if within and between-person changes in inflammation predicted cancer-related distress, intrusive thoughts, or avoidance.

## 2. Methods and materials

### 2.1 Participants and procedure

Participants were women with a breast cancer diagnosis ($n$ = 165, stages 0-IIIa) recruited from cancer clinics for a longitudinal parent study on fatigue and immune dysregulation. Sample characteristics are presented in Table 1. Women were recruited within 1-3 months after their diagnosis to complete a baseline visit before cancer treatment and two follow-up

visits 6 and 18 months after treatment ended. Visit 2 took place a little over one year ($M_{months}$ = 13.45, SD = 5.43) following the first visit while Visit 3 occurred one year following Visit 2 ($M_{months}$ = 12.10, SD = 3.33). All women provided written informed consent. Women completed self-report questionnaires and provided a blood sample at each visit. Exclusion criteria included a history of cancer except basal or squamous cell skin carcinomas and significant visual, auditory, or cognitive impairments. The Ohio State University Institutional Review Board approved the project.

### 2.2 Impact of Events Scale

The modified version of the 22-item Impact of Events Scale (IES) assessed cancer-related distress (Horowitz, Wilner, & Alvarez, 1979; Salsman, Schalet, Andrykowski, & Cella, 2015). The modified IES instructions asked the women to respond based on their recent cancer diagnosis. The total IES scale reflects global cancer related distress, and the intrusion and avoidance subscales assess two specific facets of distress.

### 2.3 Covariates

All analyses controlled for treatment type, cancer stage, physical comorbidities, body mass index (BMI), age, menopause status, depression, and visit. The Charlson comorbidity index, originally developed with breast cancer patients (Charlson, Szatrowski, Peterson, & Gold, 1994), provided data on physical comorbidities. The Charlson assigns weights to 19 medical conditions. We also controlled for depressive symptoms given previous associations between depression and inflammation along with high construct overlap with cancer-related distress and depression (Kiecolt-Glaser, Derry, & Fagundes, 2015; Valkanova, Ebmeier, & Allan, 2013). The Center for Epidemiological Studies Depression Scale (CES-D) assessed depression (Radloff, 1977).

### 2.4 Inflammation assays

Fasting blood samples were collected between 7:00 and 9:00 AM to control for diurnal variation. Serum levels of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8), and interleukin-1β (IL-1β) were measured using an electrochemiluminescence method with Meso Scale Discovery kits, and read using the Meso Scale Discovery Sector Imager 2400 (Meso Scale Discovery, Rockville, MD). Sensitivity was .3 pg/mL, .4 pg/mL, and .2 pg/mL for TNF-α, IL-6, and IL-1β, respectively. The intra-assay and inter-assay CVs for TNF-α were 4.32% and 5.30%, respectively; corresponding values were 1.43% and 4.42% for IL-6 and 4.15% and 4.03% for IL-1β. Each women's frozen samples were assayed for all cytokines in one run using the same controls for all time points for each person. Cytokine data were log transformed to better approximate normality of residuals. A z-score composite of serum cytokines was calculated to obtain a summary measure of inflammation. This method was previously used as a robust representation of overall inflammation (Alfano et al., 2017; Liu et al., 2017; Shrout et al., 2020). The z-score composite demonstrated acceptable levels of internal consistency on average across the three visits (α = .76).

### 2.5 Analytic plan

An a priori power analysis was conducted as part of the larger parent study. A power analysis using two-tailed test with a small effect and an alpha of .05 at 80% power yielded a recommended sample size of 118 survivors. SPSS Version 26 was used to conduct all analyses. Mixed linear models were used to test the study hypotheses that cancer-related distress would be linked to inflammation. The mixed models used restricted maximum likelihood estimation and accounted for the repeated assessments of each participant; a subject-specific random effect captured the within-subject correlation. Cancer-related distress and inflammation were assessed at each visit, allowing for within-person and between-person analyses. We separated out the within- and between-person effects of cancer-related distress by including the person-centered variable at level 1 and the between-person means across the study at level 2. The equations for these models are as follows:

$$\text{Level 1: Inflammation}_{\text{time i, person j}} = b_{0j} + B_1(\text{IESWI}_{ij}) + B_2(\text{IESBW}_j) + B_4(\text{Comorbid}_{ij}) + B_4(\text{BMI}_{ij}) + B_5(\text{Age}_{ij}) + B_6(\text{Depression}_{ij}) + B_7(\text{Visit}_{ij}) + B_8(\text{Stage}_j) + B_9(\text{Menopause}_{ij}) + B_{10}(\text{Treatment}_j) + e_{ij}$$

$$\text{Level 2: } b_{0j} = \gamma_{00} + u_{0j}$$

Thus, within-person cancer-related distress reflected how much higher or lower a survivor's cancer-related distress at each visit deviated from her own average across the study, whereas between-person cancer-related distress reflected her average cancer-related distress throughout the study. Separate models were run for the IES total score, the avoidance subscale, and the intrusion subscale as predictors. Each model included both the within- and between-person cancer-related distress variables. We also tested growth models where time served as the predictor of cancer-related distress, intrusive thoughts, avoidance and inflammation to examine trajectories of change across visits. Further, we also specified interactions between within-person cancer-related distress and visit to test whether the effects cancer-related distress on inflammation differed by visit. These interactions were not significant ($ps > .10$) and thus removed from the final models. All models adjusted for physical comorbidities, body mass index (BMI), age, menopause status (yes; no), depression, and visit (1; 2; 3) as time-varying (level 1) covariates, as well as treatment type (surgery only; radiation and surgery; chemotherapy and surgery; and radiation, chemotherapy, and surgery) and cancer stage (0; I; II; III) as time-invariant (level 2) covariates. Continuous covariates were grand-mean centered to improve interpretability of the intercepts. Given high construct overlap between cancer-related distress and depression, models were run both with and without depression included as a covariate. Menopause and age were significantly correlated ($r = .68$, $p < .01$). However, given that many women with breast cancer prematurely undergo menopause, we included both variables in the models to capture women who were both younger and post-menopausal. The exclusion of one of these two variables in all models did not alter any results.

# 3. Results

## 3.1 Descriptive statistics

Table 1 provides descriptive statistics and frequencies of all control variables. Table 2 presents the means and standard deviations of the IES total, the intrusion and avoidance subscales, and the inflammation composite at each visit. Zero-order correlations among study variables at Visit 1 are presented in Table 3. Overall, levels of cancer-related distress in this study resembled previous research, with it being highest at Visit 1 (post diagnosis, pretreatment), and lower following treatment (Bauer, Wiley, Weihs, & Stanton, 2017; Cordova et al., 1995). Women's mean CESD score at Visit 1 was 16.57. CESD scores reduced across visits, as 49.8% of participants had a CESD score above 16 at Visit 1,26.8% at Visit 2, and 21.2% at Visit 3.

All participants had detectable levels of IL-6, TNF-α, and IL-8 across the three visits. Detectability of IL-1β varied across the three visits. Specifically, 40 participants had IL-1β levels below detectable levels at Visit 1, 29 at Visit 2, and 11 at Visit 3. When IL-1β values were missing, the inflammatory composite was not calculated for that visit.

## 3.2 Inflammation and cancer-related distress change across time

Growth models revealed that cancer-related distress ($b = 15.08$, $SE = 1.24$, $p < .001$), intrusive thoughts ($b = 8.19$, $SE = .66$, $p < .001$), and avoidance ($b = 6.88$, $SE = .76$, $p < .001$) decreased significantly across the three study visits. Inflammation also decreased significantly across the three visits ($b = -.26$, $SE = .06$, $p < .001$). Neither cancer-related distress ($b = .003$, $SE = .002$, $p = .10$), intrusive thoughts ($b = .005$, $SE = .004$, $p = .17$), or avoidance ($b = .005$, $SE = .003$, $p = .14$) significantly predicted inflammation when added as time-varying covariates.

## 3.3 Within- and between-person cancer-related distress predicting inflammation

At the within person level, when women's own cancer-related distress was higher than usual, their inflammation was also higher ($b = .01$, $SE = .00$, $p = .01$). That is, at visits in which women had higher cancer-related distress than they typically did throughout the study, they also had higher inflammation. Cancer-related distress was not linked to inflammation at the between person level ($b = -.00$, $SE = .00$, $p = .65$). Thus, changes in women's own distress levels, but not average changes between survivors' cancer-related distress, were associated with inflammation. Removing depression from the models did not significantly change the within-person ($b = -.004$, $SE = .002$, $p = .03$) or between-person ($b = -.005$, $SE = .004$, $p = .34$) effects of cancer-related distress on inflammation.

Analyses of specific IES subscales showed relationships between avoidance and inflammation at the within-person level. When women reported greater cognitive and emotional avoidance than they usually did, they also had higher inflammation ($b = .01$, $SE = .00$, $p = .04$). Avoidance was not associated with inflammation at the between person level ($b = -.00$, $SE = .01$, $p = .62$). Within-person fluctuations in intrusive thoughts also significantly influenced inflammation ($b = .01$, $SE = .00$, $p = .03$). Intrusive thoughts were not associated with inflammation across time at the between-person level ($b = -.00$, $SE$

= .01, $p$ = .68). Thus, fluctuations in women's own avoidance and intrusion were associated with higher inflammation. When depression was removed from the models as a covariate, intrusive thoughts were not linked to inflammation at the within-person ($b$ = .01, $SE$ = .004, $p$ = .06) or between-person ($b$ = −.01, $SE$ = .01, $p$ = .25) level. Similarly, avoidance was not significantly linked to inflammation at the within-person level ($b$ = .01, $SE$ = .003, $p$ = .06), or between-person level ($b$ = −.005, $SE$ = .01, $p$ = .52) with depression removed from the models.

In addition to these main study variables, several covariates were significantly related to inflammation. Higher BMI was linked to higher inflammation ($b$ = .01, $SE$ = .01, $p$ = .05). Post-menopausal women had significantly higher inflammation ($b$ = −.20, $SE$ = .09, $p$ = .02). Physical comorbidities, depression, cancer stage, treatment, and age were not related to inflammation (all $p$s > .25).

### 3.4 Alternative Models

We also tested alternative models to assess bidirectionality. For these models, the inflammation composite variable was centered at both the between- and within-person level with cancer-related distress, avoidance, and intrusion serving as the outcome variables in separate models. Within-person changes in inflammation were significantly linked to cancer-related distress, driven by its link to intrusive thoughts rather than avoidance. Therefore, at visits where women's inflammation was higher than their own average levels, they also had more intrusive thoughts and overall cancer-related distress. Between-person changes in inflammation were not significantly linked to cancer-related distress, avoidance, or intrusive thoughts (all $p$s > .05). Comparing the Akaike information criteria (AIC) and the Bayesian information criteria (BIC) reveled a better model fit for cancer-related distress predicting inflammation, rather than the alternative models which yielded larger AlCs and BICs across models.

Although our hypotheses focused on how within-person fluctuations in cancer-related distress were related to inflammation, there can also be prospective associations between cancer-related distress and future depressive symptoms or inflammation. Separate multiple regressions were run with cancer-related distress, intrusive thoughts, or avoidance as predictors and depression or inflammation at Visits 2 and 3 as the outcome. All models controlled for Visit 1 depression or inflammation in addition to physical comorbidities, BMI, age, menopause status, cancer treatment, and stage. Cancer related distress, avoidance, and intrusive thoughts at Visit 1 did not predict depressive symptoms at Visit 2 or Visit 3 ($p$s = .10 - .84). Similarly, cancer related distress, avoidance, and intrusive thoughts at Visit 1 did not predict inflammation at Visits 2 or 3 ($p$s = .09 - .99).

## 4. Discussion

This study demonstrated that changes in cancer-related distress were linked to increased inflammation over time while controlling for depressive symptoms. At visits where a survivor's cancer-related distress was higher than her own average, her inflammation was also higher. Within-person changes in both avoidance and intrusive thoughts contributed to the association between fluctuations in cancer-related distress and inflammation. At the

between-person level, inflammation, on average, increased across study visits. However, how a woman's distress compared to other survivors (between-person differences) did not predict higher inflammation across visits. These data highlight the value of using a within-person approach to capture how a survivor's distress can influence their physical health.

Our findings have several important implications. Both intrusive thoughts and avoidance have been linked to poor adjustment throughout the cancer trajectory (Moreno et al., 2016). Previous findings highlighted intrusive thoughts as central drivers of cancer-related distress among survivors (Epping-Jordan et al., 1999). However, avoidance and intrusive thoughts both occur commonly among survivors (Bauer et al., 2017; Mehrabi, Hajian, Simbar, Hoshyari, & Zayeri, 2015). This study extends previous findings by highlighting both intrusive thoughts and avoidance as influencers of inflammation. Although intrusive thoughts and avoidance may be adaptive immediately following a cancer diagnosis, persistence during and after treatment prevents adjustment (Bauer et al., 2017; Baum, Cohen, & Hall, 1993). Our findings emphasize how intrusion and avoidance can have inflammatory consequences in addition to psychological effects throughout survivorship.

Considerable research has addressed the impact of depression and anxiety on health and well-being in a cancer context (Burgess et al., 2005). Cancer-related distress promotes anxiety and depression, which relates to heightened inflammation (Dowlati et al., 2010; Kiecolt-Glaser et al., 2015; Megan E Renna et al., 2018; Valkanova et al., 2013). This novel study demonstrated that cancer-related distress trajectories were associated with inflammatory change even while controlling for depressive symptoms. Given the link between inflammation and poor health, this study provides insight into how cancer-related distress, independent of depressive symptoms, can contribute to morbidity and early mortality in breast cancer survivorship. Notably, when depression was removed as a covariate from our models, within-person increases in avoidance and intrusive thoughts were no longer significantly linked to inflammation. In contrast, within-person increases in cancer-related distress were significantly related to inflammation even with depression removed from the models. Although avoidance and intrusive thoughts may share many commonalities with depressive symptoms, our findings highlight the unique role that cancer-related distress plays in influencing inflammation. The psychological, behavioral, and physiological mechanisms that may drive the relationship between cancer-related distress and inflammation should be explored in future research, as several mechanisms may underlie these results. For example, women who experience high rates of avoidance and intrusive thoughts may be more sedentary, suffer from sleep disturbances, be less likely to exercise, and make poor dietary choices as a means of reducing distress, thereby heightening inflammation.

These results underscore the need for screening for and treating distress in breast cancer survivors, in line with recommendations from the American Society of Clinical Oncology and accreditation standards for cancer facilities set forth by the American College of Surgeons Commission on Cancer (Andersen et al., 2014; CoC, 2019). Avoidance and intrusive thoughts both represent responses to intense emotional experiences. Such responses can be specifically targeted through treatment, ultimately reducing distress and improving a

woman's physical health and overall wellbeing (Aguirre-Camacho et al., 2017; Antoni et al., 2006).

Indeed, several psychological interventions have proven effective in reducing distress, avoidance, and intrusive thoughts among healthy adults (e.g., Acceptance and Commitment Therapy, Cognitive Behavioral Therapy, Emotion Regulation Therapy) (Hayes, Pistorello, & Levin, 2012; Megan E. Renna, Quintero, Fresco, & Mennin, 2017; Tatrow& Montgomery, 2006). Cognitive behavioral therapy can also reduce inflammation (Shields, Spahr, & Slavich,2020). Treating distress using established interventions is therefore likely to improve not only psychological health but the vast constellation of conditions caused by increased inflammation as well.

This study had several notable strengths. First, this study's design allowed us to test how inflammation and cancer-related distress changed from diagnosis to 18 months after treatment. Our longitudinal design provided a way to examine both within- and between-person changes in cancer-related distress. Utilizing an inflammatory composite variable demonstrated links between cancer-related distress and inflammation across several inflammatory markers (Liu et al., 2017). Though the current study showed that cancer-related distress was linked to inflammation after adjusting for BMI, age, physical comorbidities, depression, cancer stage and treatment, limitations include the fact that the women were not particularly diverse in terms of race and ethnicity. Additionally, although treatment (e.g., radiation or chemotherapy) decreases inflammation by reducing tumor burden, the short-term aftermath of these treatments may actually be proinflammatory in nature, with some research indicating that the cytokine cascade associated with treatment may last for months or years after treatment completion (Cirulli et al., 2015; Herskind, Bamberg, & Rodemann, 1998; Solomayer et al., 2003; Stone, Coleman, Anscher, & McBride, 2003; Wiley, Bower, Petersen, & Ganz, 2017). Despite this strength, the physiologic basis for increased inflammation observed in this study is unclear. Demonstrating how within-person fluctuations in cancer-related distress influences inflammation provides novel information of how intrusive thoughts and avoidance influence health. However, this study was correlational and we therefore were not able to assess causality between cancer-related distress and inflammation.

Cancer-related distress is an important driver of one's wellbeing following a cancer diagnosis in addition to having a strong influence on inflammation. This longitudinal study demonstrated how fluctuations in cancer-related distress may promote higher inflammation. When survivors experienced more intrusive thoughts and avoidance than what was typical for them, their inflammation was higher. This research shows how examining changes in a survivor's own cancer-related distress may be linked to risks for her own long-term health; the same information could not be gleaned from examining average change across survivors.

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## Highlights

- Breast cancer survivors provided blood samples at three visits to test for inflammation
- Survivors completed a measure of cancer-related distress at each visit
- Within-person fluctuations in cancer-related distress were linked to higher inflammation
- Between-person differences in cancer-related distress was not linked to inflammation
- We show how cancer-related distress may impact physical health among survivors

**Table 1**

Baseline characteristics of breast cancer survivors (N= 165).

| | Mean (SD) | Number (%) |
|---|---|---|
| Age | 56.83 (11.54) | |
| BMI | 29.06 (7.34) | |
| Physical comorbidities | .84 (1.38) | |
| Depression | 16.57 (7.66) | |
| Race | | |
| White | | 131 (78.9%) |
| Black | | 24 (14.5%) |
| Asian American | | 7 (4.2%) |
| Other | | 4 (2.4%) |
| Cancer stage | | |
| 0 | | 28 (16.9%) |
| I | | 78 (47.0%) |
| II | | 41 (24.9%) |
| III | | 18 (10.8%) |
| Cancer treatment | | |
| Surgery only | | 51 (30.7%) |
| Radiation and surgery | | 42 (25.3%) |
| Chemotherapy and surgery | | 28 (16.9%) |
| Radiation, chemotherapy, and surgery | | 43 (25.9%) |
| Began endocrine therapy | | 105 (63.6%) |
| No longer menstruating | | 106 (64%) |

Note. SD = standard deviation, BMI = body mass index. Depression was measured using the Center for Epidemiological Studies- Depression scale. Women who began endocrine therapy did so between visits 1 and 2.

**Table 2**

Study variable means and standard deviations (N= 165)

| | Visit 1 | Visit 2 | Visit 3 |
|---|---|---|---|
| IES total score | 27.30 (17.2) | 16.05 (15.0) | 13.70 (14.4) |
| Avoidance subscale | 14.94 (9.6) | 9.46 (8.9) | 8.40 (9.1) |
| Intrusion subscale | 12.36 (9.4) | 6.58 (7.5) | 5.29 (6.6) |
| IL-6 | 2.00 (2.33) | 2.34 (2.29) | 2.60 (2.25) |
| TNF-α | 6.90 (3.70) | 7.32 (3.26) | 7.97 (4.11) |
| IL-8 | 8.73 (6.27) | 12.49 (10.55) | 11.43 (7.62) |
| IL-1β | .95 (1.13) | .93 (1.02) | 1.04 (1.20) |

*Note.* IES = Impact of Events Scale, IL-6 = interleukin 6, TNF-α = tumor necrosis factor alpha, IL-8 = interleukin 8, IL-1β = interleukin 1-beta. Cytokine data represent non-log transformed values for individual markers. These markers were log transformed, standardized, and averaged to create the inflammatory composite measure.

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**Table 3**

Baseline correlations among study variables.

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. IES | - | | | | | | | | | | | | | | |
| 2. Intrusion | .89** | - | | | | | | | | | | | | | |
| 3. Avoidance | .88** | .57** | - | | | | | | | | | | | | |
| 4. Depression | .60** | .65** | .41** | - | | | | | | | | | | | |
| 5. TNF | .04 | .01 | .05 | .01 | - | | | | | | | | | | |
| 6. IL-6 | .02 | .01 | .03 | .08 | .60** | - | | | | | | | | | |
| 7. IL-1b | .11 | .15 | .05 | .21* | .29** | .15 | - | | | | | | | | |
| 8. IL-8 | −.01 | −.07 | .05 | −.02 | .67** | .40** | .33** | - | | | | | | | |
| 9. Composite | .04 | .04 | .03 | .09 | .79** | .72** | .66** | .45** | - | | | | | | |
| 10. Age | −.26** | −.30** | −.15* | −.30** | .14** | −.03 | −.03 | .07 | .06 | - | | | | | |
| 11. Comorbidities | .00 | .03 | −.02 | .01 | .03 | .04 | .08 | .01 | .06 | .19** | - | | | | |
| 12. BMI | .12 | .08 | .13 | .14* | .10 | .17* | −.05 | −.04 | .12 | .02 | .04 | - | | | |
| 13. Menopause | −.05 | −.09 | .01 | −.09 | .16* | .02 | .10 | .18* | .14* | .68** | .13 | .12 | - | | |
| 14. Cancer Tx | .05 | .10 | −.02 | .12 | −.11 | −.03 | .03 | −.19** | −.06 | −.15* | .02 | .08 | −.12 | - | |
| 15. Stage | .03 | .01 | .04 | .02 | −.01 | −.03 | −.09 | −.05 | −.06 | −.02 | .00 | .20** | .01 | .45** | - |

Note.

*$p < .05$

**$p < .001$

IES = Impact of Events Scale, IL-6 = interleukin 6, TNF-α = tumor necrosis factor alpha, IL-8 = interleukin 8, IL-1β = interleukin 1-beta, BMI = body mass index, Cancer Tx = cancer treatment type, Stage = cancer stage. Depression was measured using the Center for Epidemiological Studies- Depression scale.