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Multidimensional Survivorship Profile in Breast Cancer Survivors: Sleep, Functioning, Body Composition, and Inflammation

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Abstract

Purpose:

Breast cancer survivorship may involve persistent changes across multiple health domains, yet these domains are often studied in isolation. This study evaluated sleep, psychosocial health, body composition, and inflammatory biomarkers among breast cancer survivors (BCS) compared with women without a history of cancer (WHC).

Methods:

This cross-sectional study included 120 women (60 BCS and 60 WHC). Sleep and psychosocial health were assessed with validated questionnaires. Body composition was measured by dual-energy X-ray absorptiometry, and hs-CRP, IL-1β, IL-6, and TNF-α were quantified using high-sensitivity immunoassays. Multivariable regression models were adjusted for relevant covariates. Exploratory analyses examined associations among these domains in BCS.

Results:

BCS had poorer sleep quality and lower sleep efficiency than WHC, along with differences in waist circumference and selected inflammatory markers. After adjustment, survivorship status remained independently associated with poorer sleep quality, lower sleep efficiency, impaired role functioning, and lower total body fat percentage. BCS had threefold higher odds of detectable IL-1β than WHC. Exploratory analyses showed limited and heterogeneous associations among body composition, inflammation, and psychosocial factors in BCS.

Conclusions:

BCS demonstrated a domain-specific survivorship profile, exhibiting the most consistent differences in sleep and functional well-being rather than in generalized alterations across psychosocial, body composition, or inflammatory domains.

Implications for Cancer Survivors:

Survivorship care may benefit from targeted assessments of sleep and functional well-being alongside physical and biological indicators. Longitudinal research is needed to clarify how these domains interact over time and to determine whether targeted interventions improve survivorship outcomes.

Clinical Trial Registration

Clinical trial number: not applicable

Introduction

Breast cancer is the most commonly diagnosed cancer among women worldwide, and advances in early detection and treatment have substantially improved survival rates in recent decades [1]. Consequently, the population of breast cancer survivors continues to grow, shifting the focus of oncology care beyond survival toward long-term health, functional recovery, and quality of life [2, 3]. Despite these advances, many survivors experience persistent physical and psychological concerns after treatment, including fatigue, anxiety, depressive symptoms, sleep disturbances, and reduced health-related quality of life[4, 5]. Sleep disturbance is particularly prevalent and clinically relevant in breast cancer survivorship [6]. Poor sleep quality and insomnia may persist for years after diagnosis and treatment and are associated with impaired emotional functioning, cognitive performance, fatigue, and overall well-being [7, 8]. Breast cancer survivors have also reported poorer sleep outcomes than women without a history of cancer, including during long-term survivorship [9]. Sleep disruption is further associated with anxiety, depressive symptoms, and diminished quality of life, contributing to a greater overall symptom burden [10, 11].

Emerging evidence suggests that body composition and systemic inflammation may also influence health outcomes during breast cancer survivorship; however, findings remain inconsistent across biomarkers and body composition measures [12, 13]. Inflammatory biomarkers, including C-reactive protein (CRP), interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), have been associated with sleep disturbances, fatigue, depressive symptoms, and reduced quality of life among cancer survivors, although the strength and consistency of these associations vary [14–16]. Likewise, excess adiposity and unfavorable body-composition profiles, characterized by increased fat mass and reduced muscle mass, have been associated with low-grade inflammation and functional limitations among cancer survivors and individuals without a history of cancer [17, 18].

However, relatively few studies have examined sleep, psychosocial health, body composition, and inflammatory biomarkers simultaneously in breast cancer survivors and women without a history of cancer. This multidomain perspective may be particularly relevant in populations with a high prevalence of obesity, including Mexican and other Latin American women [19]. Consequently, the extent to which breast cancer survivorship is associated with differences across behavioral, psychological, and biological domains, and how these domains relate to one another during survivorship, remains incompletely understood. Therefore, this study aimed to (1) compare sleep quality, mental health outcomes, health-related quality of life, body composition, and inflammatory biomarkers between breast cancer survivors and women without a history of cancer and (2) examine associations of body composition and inflammatory biomarkers with psychosocial health outcomes and health-related quality of life among breast cancer survivors.

Methods

Study Design and Participant Selection

This cross-sectional study included breast cancer survivors (BCS) and women without a history of cancer (WHC). Participants were recruited through convenience sampling in Hermosillo, Sonora, Mexico, between June and December 2024. Eligible WHC participants were women aged ≥ 25 years with no prior cancer diagnosis. The BCS group included women who were 6 months to 5 years post-hospital treatment at the time of recruitment.

The study followed the ethical standards of the institutional research committee and the 2013 Declaration of Helsinki. The Ethics Committee of the Centro de Investigación en Alimentación y Desarrollo (CIAD) approved the study (Approval No. CEI/015 – 2/2022). Written informed consent was obtained from all participants before enrollment.

Measures

Sociodemographic and Clinical Characteristics

Sociodemographic and clinical data were collected using standardized questionnaires and, when appropriate, through medical record abstraction. Collected information included age, educational attainment, marital status, menopausal status, occupation, socioeconomic status, smoking habits, alcohol consumption, comorbid conditions, and medication use. Socioeconomic status was assessed using a questionnaire developed and validated by the Asociación Mexicana de Agencias de Investigación de Mercado y Opinión Pública [20].

Sleep Quality Assessment

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a validated 19-item questionnaire that evaluates sleep quality over the previous month. The PSQI comprises seven components, each scored 0 to 3. Global scores range from 0 to 21, with higher scores indicating poorer sleep quality. The PSQI has demonstrated high validity and reliability, with a sensitivity of 89.6%, specificity of 86.5%, and a kappa coefficient of 0.75 [21].

Anthropometric and Body Composition Measurements

Trained research personnel conducted anthropometric and body composition assessments using standardized protocols. Body weight was measured to the nearest 0.1 kg on a calibrated digital scale, and height to the nearest 0.1 cm on a wall-mounted stadiometer, following Jelliffe [22]. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m²). Waist

circumference was measured at the midpoint between the lowest rib and the iliac crest with a non-elastic anthropometric tape, following guidelines established by the International Society for the Advancement of Kinanthropometry (ISAK) [23]. Body composition was assessed using dual-energy X-ray absorptiometry (DXA) with a Hologic scanner, following standardized procedures to ensure measurement accuracy [24]. DXA measurements included total fat mass, body fat percentage, lean mass, and visceral adiposity. Trained technicians calibrated the DXA daily in accordance with manufacturer recommendations before all scans.

Inflammatory Biomarker Assessment

Venous blood samples were collected in the morning after an overnight fast of at least 8 hours. Blood was drawn into anticoagulant-containing tubes, immediately centrifuged after collection, aliquoted, and stored at − 80°C until analysis. The inflammatory biomarkers evaluated included high-sensitivity C-reactive protein (hs-CRP), interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α).

Serum hs-CRP levels were measured in duplicate using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (ab99995; Abcam, Cambridge, UK) following the manufacturer's instructions. Circulating levels of IL-1β, IL-6, and TNF-α were quantified using the BD Cytometric Bead Array (CBA) Enhanced Sensitivity Flex Sets, specifically the Human IL-1β Enhanced Sensitivity Flex Set (Cat. No. 561509), Human IL-6 Enhanced Sensitivity Flex Set (Cat. No. 561512), and Human TNF Enhanced Sensitivity Flex Set (Cat. No. 561516). These kits were used with the Enhanced Sensitivity Human Soluble Protein Master Buffer Kit (Cat. No. 561521) (BD Biosciences, San Jose, CA, USA) in accordance with the manufacturer's protocols. Samples were analyzed on a FASC Aria III, and cytokine concentrations were determined using FCAP Array version 3.0 software. According to the manufacturer, the theoretical limits of detection (LODs) were 48.4 fg/mL for IL-1β, 68.4 fg/mL for IL-6, and 67.3 fg/mL for TNF-α. For consistency and enhanced interpretability, cytokine concentrations measured in femtograms per milliliter (fg/mL) with FCAP Array software were converted to picograms per milliliter (pg/mL) and are reported throughout this document in pg/mL. Accordingly, the corresponding LODs were 0.0484 pg/mL for IL-1β, 0.0684 pg/mL for IL-6, and 0.0673 pg/mL for TNF-α.

Psychosocial Health and Quality of Life Assessment

Psychosocial health variables were assessed using validated self-report questionnaires. A high score indicates a clinically significant likelihood of a disorder. Anxiety symptoms were assessed with the Generalized Anxiety Disorder-2 (GAD-2), a brief two-item screening instrument measuring anxiety over the preceding two weeks. Each item is scored from 0 (“not at all”) to 3 (“nearly every day”), yielding a total score from 0 to 6. The GAD-2 has demonstrated a sensitivity of 86% and a specificity of 83% [25].

Depressive symptoms were assessed with the Patient Health Questionnaire-2 (PHQ-2), which evaluates depressive symptoms over the past two weeks. Each item is scored from 0 to 3, yielding a total score from 0 to 6. The PHQ-2 has demonstrated a sensitivity of 83% and a specificity of 92% [26].

Health-related quality of life (HRQL) was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, version 3.0 (EORTC QLQ-C30). This comprehensive 30-item instrument includes a global quality-of-life assessment, five functional scales (physical, role, emotional, cognitive, and social functioning), and symptom scales addressing fatigue, insomnia, and appetite loss. All scale scores were linearly transformed to a 0–100 scale in accordance with EORTC scoring guidelines. Higher scores on functional and global health scales indicate better functioning and quality of life, whereas higher symptom scores indicate a greater symptom burden. The EORTC QLQ-C30 has been validated and demonstrates high reliability, with a Cronbach's alpha of 0.89 [27].

Statistical Analysis

Descriptive statistics summarized participant characteristics and study variables. Continuous variables were presented as means ± standard deviations or medians with interquartile ranges, depending on their distribution, whereas categorical variables were expressed as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test and graphical methods. Between- group differences were analyzed using independent- samples t- tests or Mann–Whitney U tests for continuous variables and chi-square tests for categorical variables, as appropriate. Effect sizes were calculated using Cohen' s d for parametric comparisons and the rank- biserial correlation for nonparametric tests. Before conducting regression analyses, the assumptions of linearity, independence, homoscedasticity, and residual normality were verified, and multicollinearity and interaction effects were assessed. The association between breast cancer survivorship status and continuous outcomes was examined using multivariable linear regression models adjusted for age, menopausal status, alcohol consumption, comorbidities, medication use, educational attainment, employment status, and marital status. Regression coefficients (β) and 95% confidence intervals (95% CIs) were reported. Because a considerable proportion of cytokine measurements fell below the assay- specific detection thresholds, IL- 1 β, IL- 6, and TNF- α were dichotomized according to manufacturer- defined cutoffs. Their relationships with survival status were evaluated using multivariable logistic regression models with consistent covariate adjustments, and the results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Additionally, exploratory multivariable linear regression analyses within the breast cancer survivor cohort examined associations among body composition, inflammatory biomarkers, and psychosocial outcomes. All models were adjusted for menopausal status, alcohol consumption, comorbidities, and medication use. Statistical analyses were conducted using IBM SPSS Statistics version 30, with the significance threshold set at $p < 0.05$.

Results

Participant Characteristics

A total of 120 women participated in the study, including 60 breast cancer survivors (BCS) and 60 women without a history of cancer (WHC). Table 1 presents participant characteristics. Breast cancer

survivors were more likely to be postmenopausal and to report medication use than women without a history of cancer. No significant differences were observed between the groups in age, alcohol consumption, comorbidity status, marital status, economic status, educational level, or employment status.

Table 1. Participants' characteristics.

Characteristic	Total Sample (n=120)	WHC (n = 60)	BCS (n = 60)	p-value
Age (years), mean ± SD	52.5 ±9.3	52.13 ± 9.2	52.9 ± 9.4	0.65
Alcohol use, n (%)				
-Yes	62(51.7)	34(56.7)	28(46.7)	0.27
-No	58(48.3)	26(43.3)	32(53.3)	
Comorbidities, n (%)				
-Yes	89(74.2)	42(70)	47(78.3)	0.29
-No	31(25.8)	18(30)	13(21.7)	
Medication Use. n (%)				
-Yes	80(66.7)	31(51.7)	49(81.7)	<0.01
-No	40(33.3)	29(48.3)	11(18.3)	
Menopausal status, n (%)				
-Pre	33 (27.5)	24 (40)	9 (15)	0.01
-Post	87 (72.5)	36 (60)	51 (85)	
Marital status n (%)				
-Single	45 (37.5)	18 (30)	27 (45)	0.09
-Live with partner	75 (62.5)	42 (70)	33 (55)	
Economic status n(%)				
-Low	48 (40)	27 (46.6)	21 (36.8)	
-Medium	42 (35)	18 (31)	24 (42.1)	0.44
-High	25 (20.8)	13 (22.4)	12 (21.1)	
-Missing value	5 (4.2)			
Education Level, n (%)				
-Basic Education	36(30)	24(40)	12(20)	
-High School or Equivalent	43(35.8)	19(31.7)	24(40)	0.06
-College/University Education	41(34.2)	17(28.3)	24(40)	
Employment Status, n (%)				
-Employed	63(52.5)	29(48.3)	34(56.7)	0.36

-Not employed	57(47.5)	31(51.7)	26(43.3)	

Sleep Quality, Mental Health, and Health-Related Quality of Life

Table 2 compares sleep quality, mental health, and health-related quality of life between the BCS and WHC groups. Compared with the WHC group, BCS participants reported significantly poorer sleep quality and lower sleep efficiency, with small-to-moderate effect sizes. No significant between-group differences were observed in sleep duration, depressive symptoms, anxiety, overall health-related quality of life, functional domains, or symptom scales. Effect sizes for the non-significant outcomes were generally minimal, indicating limited differences between the groups across most psychosocial variables and quality-of-life indicators.

Table 2. Comparison of sleep quality, mental health, and health-related quality of life outcomes

Characteristic	**WHC (n = 60)**	**BCS (n = 60)**	**Effect sizes**	**p-value**
Sleep Quality Score, mean ± SD	7.4 ± 3.9	8.8 ± 4.2	-0.37	**0.04**
Sleep duration (h/night)	6.1 ± 1.5	5.7 ± 1.6	0.24	0.17
Sleeping efficiency (%)	81.2 (64.4-93.6)	68.9(53.3-83.9)	0.25	**0.01**
Depression score	1(0-2)	0.5(0-2)	0.05	0.59
Anxiety score	1(0-2)	1(0-2)	0.08	0.40
Global Quality of Life score	79.2 (66.7-91.7)	83.3 (66.7-91.7)	0.06	0.52
Physical Functioning score	100 (93.3-100)	93.3 (86.7-100)	0.14	0.15
Role Functioning score	100 (100-100)	100 (100-100)	0.002	0.97
Emotional Functioning score	83.3 (68.7-91.7)	83.3(68.7-100)	0.04	0.62
Cognitive Functioning score	83.3 (70.8-100)	83.3 (66.7-100)	0.06	0.53
Social Functioning score	100 (100-100)	100 (100-100)	0.13	0.13
Fatigue Symptom score	11.1 (0-22.2)	11.1 (0-22.2)	0.17	0.06
Pain Symptom score	8.3 (0-16.7)	8.3 (0-16.7)	0.02	0.83
Insomnia Symptom score	0 (0-33.3)	0 (0-33.3)	0.05	0.56
Appetite Loss Symptom score	0 (0-0)	0 (0-0)	0.05	0.58

Data are presented as mean ± SD or median (Q1-Q3), as appropriate. Between-group comparisons were conducted using independent-samples t-tests or Mann–Whitney U tests. Effect sizes are reported as

Cohen's d for normally distributed variables and as rank-biserial correlation (r) for non-normally distributed variables.

Inflammatory Biomarkers, Anthropometric, and Body Composition Measures

Table 3 presents intergroup comparisons of inflammatory biomarkers, anthropometric measurements, and body composition. The BCS group exhibited a significantly smaller waist circumference than the WHC group. Furthermore, the BCS group demonstrated higher levels of IL-1β and TNF-α; however, no significant differences were observed in BMI, total body mass, fat-free mass, body fat percentage, IL-6, or C-reactive protein. Effect sizes were predominantly small to moderate.

Table 3. Comparison of inflammatory biomarkers, anthropometric, and body composition

Characteristic	WHC (n = 60)	BCS (n = 60)	Effect sizes	p-value
Body Mass Index (kg/m²), mean ± SD	31.5 ± 6.0	29.7 ± 5.5	0.31	0.08
Waist circumference (cm), mean ± SD	100.5 ± 11.9	95.3 ± 11.4	0.44	**0.01**
Total mass (kg)	76.0 ±14.7	73.3± 13.8	0.19	0.29
Total Fat-free mass (kg)	42.2 ± 7.8	40.9 ± 6.5	0.17	0.34
Total body fat (%)	44.3 ± 4.3	43.8 ± 4.4	0.12	0.49
IL-1b (pg/mL)	0 (0-0)	0 (0-0.04)	0.20	**0.02**
IL-6 (pg/mL)	0.6 (0-3.4)	0.2 (0-1.9)	0.07	0.46
TNFa (pg/mL)	0 (0-0)	0 (0-0.2)	0.21	**0.02**
PCR (mg/L)	8.4 (4.1-20.9)	11.1 (4.2-19.9)	0.09	0.33

Data are presented as mean ± SD or median (Q1-Q3), as appropriate. Between-group comparisons were conducted using independent-samples t-tests or Mann–Whitney U tests. Effect sizes are reported as Cohen's d for normally distributed variables and as rank-biserial correlation (r) for non-normally distributed variables.

Multivariable Associations Between Breast Cancer Survivorship Status and Study Outcomes

Tables 4a and 4b summarize the multivariable regression analyses examining the relationship between breast cancer survivorship status and the study outcomes. After adjustment for sociodemographic and clinical covariates, BCS was independently associated with impaired sleep quality, reduced sleep efficiency, and lower role functioning. BCS was also associated with a lower total body fat percentage, with a borderline association observed for waist circumference. No significant adjusted associations were identified for sleep duration, depressive symptoms, anxiety, global health-related quality of life,

other functional or symptom domains, body mass index, total mass, fat-free mass, or C-reactive protein (Table 4a). In addition, with WHC as the reference group, BCS as the exposure group, and detectable IL as the outcome event, an OR of 3.24 indicates that BCS was associated with threefold higher odds of detectable IL compared with WHC (Table 4b). Collectively, these findings indicate a selective, multidimensional pattern characterized by domain-specific differences in sleep outcomes, role functioning, adiposity measures, and IL-1β detectability, without evidence of broad psychosocial impairment or systemic inflammatory differences.

Table 4a. Multivariable Associations Between Breast Cancer Survivorship Status and Study Outcomes

Outcomes	Crude β (95% CI)	Adjusted β (95% CI)	p-value
Sleep Quality Score, mean ± SD	1.48(0.02-2.94)	1.86 (0.15-3.56)	**0.03**
Sleep duration (h/night)	-0.39([-0.95]- 0.18)	-0.53([-1.21] – 0.13)	0.11
Sleeping efficiency (%)	-9.46([-16.44] – [-2.47])	-11.02([-18.9] – [-3.05])	**0.01**
Depression score	-0.1([-0.54]- 0.34)	-0.17([-0.68]- 0.33)	0.49
Anxiety score	-0.1([-0.57]- 0.37)	0.14([-0.39] – 0.68)	0.59
Global Quality of Life score	2.5([-4] - 9)	0.08([-7.12]- 7.29)	0.98
Physical Functioning score	-3.33([-7.71]- 1.05)	-3.28([-8.30]- 1.73)	0.19
Role Functioning score	-6.89([-11.02]-[-2.76])	-7.93([-12.75]- [-3.11])	**0.01**
Emotional Functioning score	1.67 ([-5.32]- 8.66)	3.38([-4.66]- 11.42)	0.41
Cognitive Functioning score	-3.61([-10.88] – 3.65)	-2.29([-10.8]- 6.24)	0.59
Social Functioning score	-1.11([-3.81]- 1.59)	-0.52([-3.6]- 2.6)	0.74
Fatigue Symptom score	4.07([-2.08]- 10.23)	2.27([-4.79]- 9.33)	0.52
Pain Symptom score	0.83([-6.7]- 8.39)	-1.41([-10.12]- 7.3)	0.75
Insomnia Symptom score	1.67([-8.23]- 11.56)	0.15([-11.43]- 11.72)	0.98
Appetite Loss Symptom score	-1.67([-6.36]- 3.03)	1.29([-4.06]- 6.64)	0.63
Body Mass Index (kg/m²), mean ± SD	-1.79([-3.87]- 0.28)	-1.5([-3.94]- 0.88)	0.21
Waist circumference (cm), mean ± SD	-5.15([-9.37]- [-0.93])	-4.69([-9.41]- 0.04)	0.05
Total mass (kg)	-2.76([-7.92]- 2.4)	-1.11([-6.95] – 4.73)	0.71
Total Fat-free mass (kg)	-1.25([-3.85]- 1.35)	0.66([-2.20] – 3.51)	0.65
Total body fat (%)	-0.55([-2.12]- 1.02)	-1.86([-3.61]- [-0.10])	**0.03**
PCR (mg/L)	0.24([-0.59]- 1.07)	0.27([-0.71]- 1.26)	0.58

Values represent adjusted regression coefficients (β) and 95% confidence intervals (CI) estimated from multivariable linear regression models. Models were adjusted for age, menopausal status, alcohol consumption, comorbidities, medication use, educational level, employment status, and marital status.

Table 4b. Multivariable Associations Between Breast Cancer Survivorship Status and Study Outcomes

Outcomes	OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
IL-1β	3.24 (1.24 – 8.49)	0.02	7.79 (1.91 – 31.72)	**0.004**
IL-6	0.87 (0.42 -1.79)	0.71	1.22 (0.49- 2.97)	0.67
TNF-α	2.76 (1.24 – 6.14)	0.01	2.19 (0.84 – 5.77)	0.11

Values represent adjusted odds ratios (ORs) and 95% confidence intervals (CIs) estimated using multivariable logistic regression models. IL-1β, IL-6, and TNF-α were analyzed as binary variables according to the assay-specific limits of detection (LODs) reported by the manufacturer. For IL-1β, concentrations <0.0484 pg/mL were classified as below the LOD (coded as 0) and concentrations ≥0.0484 pg/mL as at or above the LOD (coded as 1). Corresponding thresholds were <0.0684 versus ≥0.0684 pg/mL for IL-6 and <0.0673 versus ≥0.0673 pg/mL for TNF-α. These thresholds were used solely for analytical classification of cytokine detectability and do not represent clinically validated cut-off values. Models were adjusted for age, menopausal status, alcohol consumption, comorbidities, medication use, educational level, employment status, and marital status. Values below the LOD should not be interpreted as true zero concentrations.

Exploratory Associations Within the Breast Cancer Survivor Group

Exploratory multivariable analyses were conducted exclusively among breast cancer survivors to examine associations between body composition, inflammatory biomarkers, and psychosocial and health-related quality-of-life outcomes (Supplementary Table S1). All models were adjusted for menopausal status, alcohol use, comorbidities, and medication use. Given the exploratory nature of these analyses, the large number of statistical tests, and the lack of multiple-comparison adjustment, interpret the findings cautiously. Overall, body composition measures and inflammatory biomarkers demonstrated limited and inconsistent associations with psychosocial health and health-related quality-of-life outcomes. Although several statistically significant associations were observed across specific symptom domains, including sleep quality, fatigue, pain, and insomnia, these findings were not consistently replicated across related outcomes or exposure variables. Collectively, the results do not support a generalized relationship between body composition, inflammatory biomarkers, and psychosocial functioning among breast cancer survivors. Rather, they suggest domain-specific associations that warrant confirmation in larger prospective studies.

Discussion

This study identified a selective pattern of health differences among breast cancer survivors (BCS), with sleep and functional outcomes emerging as the most consistent domains distinguishing BCS from women without a history of cancer (WHC). BCS exhibited poorer sleep quality, lower sleep efficiency, and reduced role functioning, and these differences persisted after adjustment for relevant demographic and

clinical characteristics. In contrast, depression, anxiety, and global quality of life did not differ significantly between groups. Differences in body composition were modest, whereas inflammatory findings were heterogeneous, with the most notable adjusted finding being approximately threefold higher odds of detectable interleukin-1β (IL-1β) among BCS. Exploratory analyses within BCS did not reveal a consistent pattern linking body composition, inflammatory biomarkers, and psychosocial outcomes. Taken together, these findings suggest that survivorship-related differences may be domain-specific rather than uniformly expressed across psychological, functional, anthropometric, and biological outcomes.

Sleep quality was the most consistent domain distinguishing BCS from WHC. BCS reported poorer sleep quality and lower sleep efficiency. After adjusting for relevant demographic and clinical characteristics, survivorship status remained independently associated with poorer sleep quality. These findings align with evidence that sleep disturbance is common among breast cancer survivors and may persist beyond completion of primary treatment [28, 29]. Persistent sleep problems are clinically relevant because they may coexist with fatigue, impaired daily functioning, psychological symptoms, and reduced quality of life, potentially affecting survivors' ability to resume or maintain usual social and occupational roles [30].

The concurrent reduction in role functioning further underscores the importance of sleep and functional well-being in survivorship care. Although the cross-sectional design prevents determining whether poorer sleep contributes to reduced functioning, whether functional limitations affect sleep, or whether both reflect other survivorship-related factors, their coexistence identifies a clinically relevant area for assessment. Importantly, sleep should not be assumed to simply reflect generalized psychological distress, because depression, anxiety, and global quality of life did not differ significantly between groups in this study. Instead, sleep may represent a distinct survivorship concern that warrants direct assessment.

From a supportive-care perspective, these findings support incorporating sleep and functional assessments into comprehensive breast cancer survivorship care, particularly for survivors reporting fatigue, difficulty with daily activities, or reduced well-being. Identifying persistent sleep problems may offer an opportunity to address potentially modifiable contributors to impaired functioning through appropriate symptom management or behavioral interventions. However, longitudinal studies are needed to determine whether changes in sleep precede changes in functioning and whether sleep-targeted interventions can improve broader survivorship outcomes.

In contrast to the differences observed in sleep and role functioning, depression, anxiety, and global quality of life did not differ significantly between BCS and WHC. These findings suggest that survivorship should not necessarily be characterized by uniformly poorer psychosocial health. Psychological outcomes may vary by time since treatment, disease characteristics, treatment exposures, menopausal status, social circumstances, coping resources, and individual adaptation to survivorship [31, 32].

The absence of significant between-group differences should not be taken as evidence that psychosocial concerns are unimportant in breast cancer survivorship. Rather, these findings support an

individualized approach in which psychosocial needs are assessed rather than assumed solely on the basis of survivorship status. This distinction is relevant to supportive care because survivors may experience persistent difficulties in specific domains, such as sleep or functioning, despite relatively preserved overall psychological well-being. A multidomain assessment may therefore help identify specific supportive-care needs that could be missed when survivorship outcomes are considered only at the level of global quality of life or psychological distress.

Differences in body composition were relatively modest. In unadjusted comparisons, BCS had a smaller waist circumference than WHC. After adjustment, survivorship status was associated with a lower percentage of total body fat, with a borderline association for waist circumference. No significant differences were observed in BMI or fat-free mass. These findings suggest modest differences in adiposity-related measures rather than broad alterations in overall body composition.

The absence of consistent differences across body-composition measures is important when interpreting the broader survivorship profile. Although excess adiposity can contribute to chronic low-grade inflammation and has been associated with cancer outcomes [33, 34], the present findings do not support a simple explanation in which overall adiposity differences account for the observed psychosocial or inflammatory findings. Body composition after breast cancer treatment is likely influenced by multiple factors, including treatment exposures, menopausal status, physical activity, dietary behaviors, medication use, and metabolic health. Future longitudinal studies that incorporate repeated measures of body composition alongside lifestyle and treatment-related characteristics may help clarify how these factors change across the survivorship trajectory.

Inflammatory findings were heterogeneous. In unadjusted analyses, BCS had higher concentrations of IL-1β and tumor necrosis factor-α (TNF-α); however, these differences were not consistently maintained after adjustment. In the adjusted analysis, BCS had approximately threefold higher odds of detectable IL-1β than WHC, whereas no significant adjusted associations were observed for IL-6, TNF-α, or C-reactive protein (CRP).

The IL-1β finding warrants cautious interpretation. Because a substantial proportion of cytokine measurements fell below assay-specific limits of detection, the adjusted analysis assessed detectability rather than absolute circulating concentrations. Therefore, the finding indicates a greater likelihood of measurable IL-1β among BCS but does not establish higher circulating IL-1β concentrations in survivors. Cancer survivorship research has similarly reported heterogeneity across inflammatory biomarkers, with associations with symptoms and quality of life varying by population and biomarker examined [35, 36].

The association between IL-1β detectability and survivorship is biologically plausible because IL-1β participates in innate immune signaling and has been implicated in sleep–wake regulation [37, 38]. However, the present findings do not establish a mechanistic relationship between IL-1β and sleep. Given the cross-sectional design and the binary analysis of IL-1β detectability, it remains unclear whether inflammatory signaling contributes to sleep disturbance, whether sleep disturbance influences inflammatory processes, or whether other survivorship-related factors influence both. Accordingly, the IL-

1β finding should be considered hypothesis-generating rather than clinically actionable and warrants confirmation in larger longitudinal studies using quantitative biomarker measurements.

The exploratory analyses conducted within BCS did not reveal a consistent pattern of associations among body composition, inflammatory biomarkers, and psychosocial outcomes. Rather than indicating a unified biological or psychosocial profile, these findings suggest that different survivorship domains may vary relatively independently across individuals. Survivorship research has similarly described heterogeneity, with symptom and quality-of-life domains not necessarily clustering consistently across survivors [39, 40].

This heterogeneity may reflect the complexity of survivorship. BCS differ substantially in treatment exposures, time since diagnosis, menopausal status, comorbidities, medication use, lifestyle behaviors, and psychosocial circumstances. These factors may contribute to distinct survivorship experiences that cannot be adequately captured by a single biological or psychosocial profile. The relatively modest sample size and exploratory nature of these analyses also limit the ability to detect smaller associations and increase the possibility that some observed associations occurred by chance. Accordingly, these exploratory findings should be interpreted as hypothesis-generating and require replication in larger studies.

From a supportive-care perspective, the most clinically relevant findings were persistent differences in sleep and role functioning. These findings support incorporating targeted sleep and functional assessments into comprehensive breast cancer survivorship care, particularly for survivors reporting fatigue, difficulties with daily activities, or reduced well-being. Importantly, sleep should be assessed alongside, rather than treated as a proxy for, psychosocial health, because poorer sleep may persist even when depression, anxiety, and global quality of life do not differ significantly between survivors and women without a history of cancer.

The findings also support a multidomain approach to survivorship assessment that identifies specific symptoms and functional concerns rather than assuming a uniform pattern of impairment across all survivors. This approach may help clinicians recognize potentially modifiable concerns and determine when additional symptom management, behavioral, psychosocial, or rehabilitative support is warranted.

In contrast, inflammatory findings are currently more relevant to research than to clinical decision-making. The association with detectable IL-1β may guide future investigation but, based on the present evidence, does not support routine inflammatory biomarker assessment in survivorship care. Larger longitudinal studies with repeated assessments of sleep, functioning, body composition, inflammatory biomarkers, treatment exposures, and symptom burden are needed to determine whether specific biological or behavioral profiles identify survivors at greater risk of persistent supportive-care needs and whether targeted interventions improve these outcomes.

Strengths and Limitations

This study has several strengths. It simultaneously examined sleep, psychosocial health, health-related quality of life, body composition, and inflammatory biomarkers, providing a multidomain characterization of breast cancer survivorship. The inclusion of women without a history of cancer provided a comparator group for evaluating survivorship-related differences. In addition, body composition was objectively assessed using dual-energy X-ray absorptiometry, and multivariable analyses accounted for relevant sociodemographic and clinical characteristics.

Several limitations should also be considered. First, the cross-sectional design precludes conclusions about temporal relationships or causality. Second, the exploratory analyses involved multiple comparisons, increasing the risk of type I error; therefore, these findings should be interpreted as hypothesis-generating. Third, assay-specific limits of detection affected cytokine analyses, particularly for IL-1β and IL-6, so detectability analyses do not provide the same information as analyses of continuous circulating concentrations. Fourth, the relatively modest sample size, particularly for analyses restricted to BCS, may have limited statistical power and contributed to imprecision in estimates. Finally, the single-center convenience sample may limit generalizability to other breast cancer survivor populations with different demographic, clinical, and survivorship characteristics. Residual confounding also cannot be excluded despite adjustment for relevant covariates.

Conclusions

Breast cancer survivorship was associated with a selective, domain-specific pattern of health differences, with the most consistent findings involving poorer sleep quality, reduced sleep efficiency, and diminished role functioning. Differences in body composition were modest, whereas inflammatory findings were heterogeneous and primarily reflected higher odds of detectable IL-1β rather than consistent elevations across inflammatory biomarkers. Depression, anxiety, and global quality of life did not differ significantly between groups.

These findings suggest that survivorship-related health differences are not uniformly expressed across psychological, functional, anthropometric, and biological domains. The prominence of sleep and functional differences underscores the potential value of incorporating sleep and functional assessments into comprehensive survivorship care. Longitudinal studies are warranted to clarify how sleep, functioning, body composition, and inflammation interact over time and to determine whether targeted supportive-care interventions can improve persistent survivorship concerns.

Declarations

Conflict Of Interest

The authors declare no conflicts of interest regarding this article's research, authorship, or publication.

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Ethical Approval

This study was conducted in accordance with the ethical standards established by the institutional research committee and the 2013 Declaration of Helsinki. The ethics committee of the Centro de Investigación en Alimentación y Desarrollo (CIAD) granted ethical approval under approval number CEI/015-2/2022. All participants provided written informed consent before participating.

Informed Consent

Participants received an informed consent form, which they signed after a full explanation of the study, and agreed to participate

Author Contribution

All authors contributed to the study's conception and design. PMN handled material preparation and data collection, analyzed the data, and drafted the initial manuscript. All authors provided feedback on earlier versions and read and approved the final manuscript.

Data Availability

The datasets generated and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Clinical Trial Registration

Clinical trial number: not applicable

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