Breast Cancer (2019) 26:758–765
https://doi.org/10.1007/s12282-019-00979-y

ORIGINAL ARTICLE

Comparison of central sensitization-related symptoms and health-related quality of life between breast cancer survivors with and without chronic pain and healthy controls

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Received: 28 January 2019 / Accepted: 17 May 2019 / Published online: 24 May 2019

Abstract

Background In breast cancer survivors, multiple risk factors for health-related quality of life (HRQoL) and chronic pain, including cancer treatment-related factors, psychosocial factors, and central sensitization (CS), have been suggested; however, there has been no comparative study between breast cancer survivors with and without pain. This study aimed to compare the demographic characteristics, psychological factors, and CS-related symptoms between breast cancer survivors with pain, those without pain, and healthy controls, and to investigate the relationships of these factors with HRQoL.

Methods We conducted a cross-sectional survey of 218 women, including patients who underwent breast cancer surgery and adjuvant therapy and healthy women.

Results Patients were divided into the pain group ($n=42$), without-pain group ($n=51$), and healthy group ($n=47$); thus, among breast cancer survivors, 45% reported chronic pain. The proportion of participants who received breast cancer treatments, such as axillary lymph node dissection and chemotherapy, was higher in the pain group than in the without-pain group ($p<0.05$). The Central Sensitization Inventory (CSI) and psychosocial factors in the pain group were higher than those in the without-pain group and healthy group ($p<0.01$). The CSI and PCS showed larger effect sizes than treatment-related factors. Moreover, HRQoL was significantly correlated with CSI, PCS, Patient Health Questionnaire-2, and Generalized Anxiety Disorder-2 scale (all, $p<0.01$). On multiple linear regression analysis, CSI accounted for 43% of the variance in HRQoL.

Conclusions CS and pain catastrophizing may be more associated with the development and/or maintenance of persistent pain than treatment-related factors.

Keywords Cancer pain · Breast cancer · Central sensitization · Central Sensitization Inventory · Quality of life

Introduction

Breast cancer is the most common cancer in women worldwide [1]. The incidence of breast cancer has increased, and the number of breast cancer survivors has also increased due to advances in medicine [2]. Although with an improved survival rate, breast cancer survivors may experience pain as a result of cancer treatment such as surgery, radiotherapy, chemotherapy, and hormone therapy [3, 4].

The prevalence of chronic pain after breast cancer treatment varies widely, ranging from 13 to > 70% [5, 6]. Problems persist for a long time even after treatment [3, 4, 7]; particularly, persistent pain leads to dysfunction of the upper limb and a decline in the survivor's activities of daily living and consequent quality of life (QoL) [7, 8]. At the early stage of breast cancer treatment, several studies reported that

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pain was mostly influenced by differences in surgery type, radiotherapy, chemotherapy, and hormone therapy [8, 9]. Pain in breast cancer is classified into inflammatory/nociceptive pain (caused by damage to tissue, bone, muscle, or connective tissue) or neuropathic pain (caused by disease or lesions involving the nerves) [10]. However, at the latter stage of breast cancer treatment, when the local effects of the different treatment modalities should have disappeared, the primary causes of pain may be overshadowed by sensitization of the central nervous system in a subgroup of breast cancer survivors [9, 11, 12]. In a recent report, Leysen et al. indicated that due to the nature of the disease and the multimodal treatment, breast cancer patients are often exposed to a mixture of nociceptive, neuropathic, and/or central sensitization (CS) pain, also called mixed pain [13]. According to the International Association for the Study of Pain, CS is defined as "increased responsiveness of the nociceptive neurons in the central nervous system to normal or subthreshold afferent input" [14]; CS is operationally defined as the amplification of neural signaling within the central nervous system that elicits pain hypersensitivity [15]. There has been increasing evidence suggesting the influence of CS, such as reduction in the pain threshold and widespread pressure-pain hyperalgesia, on persistent pain in breast cancer survivors [11, 12, 16]. Although these studies evaluated pain hypersensitivity, the main aspect of CS, through the pressure-pain threshold and temporal summation measured using Quantitative Sensory Testing (QST) [11, 12, 16], QST is a burden for clinicians because of associated high cost, complexity, and time-consuming quality [9]. Recently, the Central Sensitization Inventory (CSI) was proposed as an alternative method and a comprehensive screening tool for the evaluation of CS-related symptoms [17, 18]. CSI demonstrates good psychometric properties, clinical utility, and initial construct validity [17, 19]. CSI has been translated into many languages and validated by various experts [18, 20, 21]. One study showed that CSI was associated with dysfunction of the descending pain-modulatory system measured by a conditioned pain modulation task [20], but another study showed that CSI was not associated with remote pressure pain threshold [22]. Currently, it is unclear whether CSI measures the aspects of CS using QST or not. However, sufficient evidence has shown that CSI is useful in the evaluation of CS in patients with chronic pain and has good clinical applicability: CSI score and severity level were associated with patient-reported depressive symptoms, perceived disability, sleep disturbance, and pain intensity in people with chronic pain [18, 20, 21]. Regarding patients with breast cancer, De Groef et al. showed that 38% of participants with pain who underwent treatment for breast cancer had signs of CS evaluated using CSI [23]. However, whether CSI can be used to distinguish between breast cancer survivors with and without chronic pain remains unknown. Previous studies suggested that CS may be induced and maintained by breast cancer treatment such as surgery and chemotherapy [11, 12, 24]. Therefore, a higher CSI score may be also found in breast cancer patients who underwent surgery and have no chronic pain. Furthermore, we hypothesized that the effect size of CSI scores is larger than that of treatment type (surgery, radiotherapy, chemotherapy, and hormone therapy) in breast cancer survivors with pain than in those without pain.

Breast cancer survivors at 1 year after surgery were reported to have a lower health-related QoL (HRQoL) than age-matched healthy controls [25]. It is thus important to find HRQoL-related factors to evaluate treatment effectiveness, especially in patients with chronic pain. A previous study showed that psychological factors such as anxiety and depression were associated with lower HRQoL in patients with breast cancer [26]. In addition, among people with chronic pain, a higher CSI score was correlated with lower HRQoL [18]. Therefore, it is possible that CS-related symptoms can also influence HRQoL in breast cancer survivors. Following were the aims of this study: (1) to compare CS-related symptoms, psychological factors, and treatment type among breast cancer survivors with pain, without pain, and healthy controls, and (2) to investigate the contribution of CS-related symptoms and psychological factors to HRQoL in patients with and without chronic pain.

Methods

Study design and participants

This cross-sectional study was conducted at the Breast Care Sensyu Clinic, Kishiwada, Japan, from April 2017 to July 2018. We consecutively recruited 171 postoperative breast cancer survivors. The participants underwent surgery at least 6 months ago and completed cancer treatments such as chemotherapy and radiotherapy at least 3 months ago. Individuals who had recurrence or metastasis of cancer and/or diseases that affect HRQoL other than pain (e.g., cardiovascular and respiratory diseases) and showed poor Japanese language comprehension were excluded from data analysis. None of the patients had undergone breast reconstruction. Participants with persistent pain who scored > 0 at pain intensity items of the Brief Pain Inventory (BPI) (see "Pain intensity and pain interference") for > 3 months [27] after surgery or treatment were assigned as the pain group, and others were defined as the without-pain group. Healthy controls who were age-matched women without specific diseases such as musculoskeletal, cardiovascular, and respiratory disorders were recruited from the general population. After informed consent was obtained from the participants, an investigator (M.M.) administered questionnaires such as CSI and psychosocial evaluation. The questionnaires took

about 15 min to complete. The research staff extracted data from the patients' medical records and completed forms that measured sociodemographic and clinical characteristics such as cancer stage and surgery type. Ethical approval was obtained from the Institutional Ethics Committee of Konan Women's University. All patients provided written informed consent prior to the study. The study was conducted in accordance with the Declaration of Helsinki.

Demographic and clinical variables

Demographic variables included age, height, weight, body mass index (BMI), and years of education. In breast cancer survivors, the clinical variables for treatment-related factors included surgery type, axillary surgery, radiotherapy, chemotherapy, and hormone therapy.

Pain intensity and pain interference

Pain intensity and pain interference were measured using the BPI [28], which consists of four pain intensity items and seven pain interference items, in patients with breast cancer. These items were presented in 0–10 scales, with 0 as none and 10 as worst (completely). The individual pain intensity and pain interference scores were calculated by averaging.

CSI

The CSI is a 25-item self-report questionnaire designed to assess health-related symptoms that are common to central sensitivity syndromes (CSS). Each item is rated on a five-point Likert scale (0 = never and 4 = always), with total scores of 0–100. The CSI was divided into five categories with increasing severity—subclinical (0–29), mild (30–39), moderate (40–49), severe (50–59), and extreme (60–100)—through empirical reasoning and deduction, under the guidance of the score distributions [29]. Part B of the questionnaire queried whether one or more specific disorders, including seven separate CS-related symptoms (fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder, irritable bowel syndrome, migraine or tension headaches, multiple chemical sensitivities, and restless legs syndrome), were diagnosed previously. Translation and validation studies of the Japanese version of the CSI have been reported [21].

HRQoL

HRQoL was measured using the EuroQol 5-dimension (EQ-5D) questionnaire, which comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three grades (no problems, some problems, and extreme problems) with values expressed as numbers on a scale with 1 as full health and 0 as mortality. Tsuchiya et al. showed the Japanese value set for the questionnaire [30].

Pain-related catastrophizing

Pain-related catastrophizing was measured using the Pain Catastrophizing Scale (PCS), which consists of 13 items describing thoughts and feelings that individuals may experience when in pain (range 0–52), with higher scores corresponding to more severe catastrophic thoughts about pain [31].

Depression

Depression was measured using the Patient Health Questionnaire-2 (PHQ-2) [32]. The questions were scored using a Likert scale of 0–3, with 0 as not at all and 3 as nearly every day. Total scores ranged from 0 to 6.

Anxiety

Anxiety disorder was measured using the Generalized Anxiety Disorder-2 (GAD-2) questionnaire [33]. Questions were scored using a Likert scale of 0–3, with 0 as not at all and 3 as nearly every day. Total scores ranged from 0 to 6.

Statistical analyses

Continuous variables were expressed as means ± standard deviations and categorical variables as *N* (%). First, demographic variables, psychological evaluation, HRQoL, and CS were compared between the pain group, without-pain group, and healthy controls using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison tests to adjust for multiple comparisons. The prevalence of each CS severity level in the participants was computed, and percentages of participants with moderate to higher CS (CSI score > 40) and CS-related symptoms (CSS ≥ 1) were compared between the pain group, without-pain group, and healthy controls using Fisher's exact test. Similarly, Fisher's exact test was used to compare the breast cancer treatment-related factors (chemotherapy, radiotherapy, type of breast and axillary surgery, etc.) between the pain group and without-pain group. In each group, the effect sizes for CSI, PCS, PHQ-2, and GAD-2 were calculated using η^2 (a large effect was defined as > 0.14, a moderate effect as between 0.06 and 0.14, and a small effect as < 0.06). In the pain group and without-pain group, the effect sizes for the breast cancer treatment-related factors were calculated using Cohen's *d* for continuous variables and Cramer's *V* for categorical variables (Cohen's *d*: a large effect was defined as > 0.8, a moderate effect as between 0.5 and 0.8, and a small effect

as < 0.5; Cramer's *V*: a large effect was defined as > 0.5, a moderate effect as between 0.3 and 0.5, and a small effect as < 0.3).

Second, we evaluated the relationship between HRQoL and other variables such as CSI and PCS using Spearman's rank correlation coefficient in all subjects together. In addition, a stepwise multiple regression analysis was performed to define the contribution of the independent variables (age, education level, BMI, CSI, PCS, PHQ-2, and GAD-2) to the dependent variable (EQ-5D). Multicollinearity was assessed using the variance inflation factor (VIF) test. All statistical analyses were performed using JMP® 13 (SAS Institute Inc., Cary, NC, USA). Significance level was set at $p < 0.05$ for all statistical tests.

Results

Study population and demographic variables

People with recurrence or metastasis of cancer ($n = 5$), those undergoing radiotherapy or chemotherapy after surgery ($n = 40$), those with diseases affecting behavior other than pain such as cardiovascular disease and respiratory disease ($n = 10$), those with poor Japanese language comprehension ($n = 6$), and those who did not complete the questionnaire ($n = 17$) were excluded. As a result, 93 breast cancer survivors (mean age 56.3 ± 10.6 years; mean time after surgery: 1.6 ± 0.8 years) met the study's criteria.

Table 1 shows the participants' demographic variables. A total of 140 women, including the pain group ($n = 42$), without-pain group ($n = 51$), and healthy controls ($n = 47$), were included for analysis. There was a significant difference in education level among the three groups ($F = 4.456$, $df = 2$, $p = 0.013$), but the difference between the pain group and without-pain group was not significant ($p = 0.965$). Other demographic data showed no significant differences between the three groups.

CS, HRQoL, and psychological factors: comparison between breast cancer survivors with and without chronic pain and healthy controls

Table 2 gives an overview of the ANOVA for psychological evaluation, HRQoL, and CS, which were compared between the pain group, without-pain group, and healthy controls.

Table 1 Demographic variables of study population ($n = 140$)

	Healthy ($n = 47$)	Without pain ($n = 51$)	Pain ($n = 42$)	*p*
Age (years)	55.7 (16.9)	54.5 (9.8)	58.2 (11.2)	0.39
Height (cm)	156.6 (4.7)	156 (5.7)	155.7 (5.4)	0.67
Weight (kg)	52.9 (7.8)	55.2 (7.7)	55.4 (9.5)	0.27
BMI (kg/m^2)	21.6 (3.3)	22.8 (3.1)	22.9 (3.7)	0.12
Education (years)	13.8 (2.0)	12.8 (1.9)	12.9 (1.4)	0.013

Data are mean ± standard deviation

BMI body mass index

Table 2 Participants' psychological variables and QOL variables, CS variables ($n = 140$)

	Healthy control ($n = 47$)	Without pain ($n = 51$)	Pain ($n = 42$)	*p*	Effect size
EQ-5D	0.91 (0.12)	0.95 (0.1)	0.73 (0.11)	< 0.001	$\eta^2 = 0.42$
CSI score	14.9 (9.7)	14.1 (9.5)	26.3 (12.6)	< 0.001	$\eta^2 = 0.21$
CSI ≥ 40	1 (2.1)	0	5 (11.9)	0.008	$V = 0.25$
CSS ≥ 1	7 (14.9)	8 (15.7)	12 (28.6)	0.229	$V = 0.15$
PCS	10.2 (10.4)	14.1 (9.9)	21.7 (9.4)	< 0.001	$\eta^2 = 0.18$
PHQ-2	0.32 (0.63)	0.39 (0.92)	0.95 (1.32)	0.005	$\eta^2 = 0.07$
GAD-2	0.38 (0.8)	0.54 (1.14)	0.79 (1.03)	0.171	$\eta^2 = 0.03$
BPI intensity	–	–	3.43 (1.7)	–	–
BPI interference	–	–	2.22 (1.7)	–	–

Data are mean ± standard deviation or *N* (%)

PHQ-2 Patient Health Questionnaire-2, *GAD-2* Generalized Anxiety Disorder-2, *PCS* Pain Catastrophizing Scale, *EQ-5D* EuroQol 5-dimension, *CSI* Central Sensitization Inventory, *BPI* Brief Pain Inventory, effect sizes (η^2: a large effect was defined as > 0.14, a moderate effect between 0.06 and 0.14 and a small effect < 0.06. Cramer's *V*: a large effect was defined as > 0.5, a moderate effect between 0.3 and 0.5 and a small effect < 0.3)

Table 3 Treatment details

	Without pain ($n=51$)	Pain ($n=42$)	p	Effect size
Time after surgery (years)	1.6 (0.9)	1.6 (0.8)	0.681	$d=0.09$
Stage of cancer			0.013	$V=0.26$
0–I	34 (66.7)	18 (40.5)		
II–III	17 (33.3)	25 (59.5)		
Type of breast surgery			0.501	$V=0.09$
Mastectomy	14 (27.4)	15 (35.7)		
Breast conserving	37 (72.6)	27 (64.3)		
Axillary lymph node dissection	8 (15.7)	19 (45.2)	0.003	$V=0.33$
Chemotherapy (taxane)	13 (25.5)	21 (50.0)	0.018	$V=0.25$
Radiotherapy	38 (74.5)	29 (69.1)	0.645	$V=0.06$
Hormone therapy			0.133	$V=0.21$
No	16 (31.4)	10 (23.8)		
Aromatase inhibitor	15 (29.4)	21 (50.0)		
Selective estrogen receptor modulator	20 (39.2)	11 (26.2)		

Comparison among pain group and pain-free group ($n=93$)

Data are mean ± standard deviation or *N* (%). Effect sizes (Cohen's *d*: a large effect was defined as > 0.8, a moderate effect between 0.5 and 0.8 and a small effect < 0.5. Cramer's *V*: a large effect was defined as > 0.5, a moderate effect between 0.3 and 0.5 and a small effect < 0.3.)

There was a significant difference in HRQoL among the three groups (EQ-5D, $F=48.956$, $df=2$, $p<0.001$), CS (CSI, $F=18.37$, $df=2$, $p<0.001$), pain-related catastrophizing (PCS, $F=15.32$, $df=2$, $p<0.001$), and depression (PHQ-2, $F=5.462$, $df=2$, $p=0.0052$). There were no significant differences in anxiety among the three groups (GAD-2, $F=1.78$, $df=2$, $p=0.172$).

Post hoc Tukey's multiple comparison of effect sizes showed that the pain group had significantly lower EQ-5D score than the without-pain group and healthy controls (0.73 ± 0.11 vs 0.95 ± 0.1 vs 0.91 ± 0.12, $p<0.001$), as well as significantly higher CSI score (26.3 ± 12.6 vs 14.1 ± 9.5 vs 14.9 ± 9.7, $p<0.001$), PCS (21.7 ± 9.4 vs 14.1 ± 9.9 vs 10.2 ± 10.4, $p<0.001$), and PHQ-2 (0.9 ± 1.4 vs 0.43 ± 0.96 vs 0.32 ± 0.63, $p<0.01$). The effect sizes were large for the EQ-5D ($\eta^2=0.42$), CSI score ($\eta^2=0.21$), and PCS ($\eta^2=0.18$) and moderate for the PHQ-2 ($\eta^2=0.07$). The proportion of subjects with a CSI score > 40 was significantly higher in the pain group (11.9% vs 0% vs 2.1%, $p<0.05$), but the group had a small effect size ($V=0.25$).

Differences in cancer treatment between breast cancer survivors with and without chronic pain

Table 3 shows the breast cancer treatment-related factors. The proportion of patients was significantly higher in the pain group than in the without-pain group for the following clinical variables: stage II–III (59.5% vs 33.3%, $p=0.013$), axillary lymph node dissection (45.2% vs 15.7%, $p=0.003$), chemotherapy (50% vs 25.5%, $p=0.018$). Among them, axillary lymph node dissection showed a moderate effect size ($V=0.33$), whereas stages II–III ($V=0.26$) and chemotherapy ($V=0.25$) showed small effect sizes. There were no significant differences in the type of breast surgery, radiotherapy, and hormone therapy between the two groups ($p=0.501$, 0.645, and 0.133 respectively).

Relationship between EQ-5D, demographic variables, CSI, and psychosocial factors

In the univariate analysis, there were no significant associations between demographic variables (age and education) and HRQoL (Table 4). However, HRQoL was significantly correlated with CSI, PCS, PHQ-2, and GAD-2

Table 4 Univariate analyses of EQ-5D with CSI, PCS, PHQ-2 and GAD-2

	EQ-5D		
	Correlation coefficient	p	95% confidence interval
Age	− 0.09	0.30	− 0.26 to 0.07
Education	0.13	0.13	− 0.04 to 0.29
CSI score	− 0.63	< 0.001	− 0.74 to − 0.55
PCS	− 0.48	< 0.001	− 0.6 to − 0.34
PHQ-2	− 0.38	< 0.001	− 0.55 to − 0.28
GAD-2	− 0.37	< 0.001	− 0.52 to − 0.24

CSI Central Sensitization Inventory, *BPI* Brief Pain Inventory, *EQ-5D* EuroQol 5-dimension, *PCS* Pain Catastrophizing Scale, *PHQ-2* Patient Health Questionnaire-2, *GAD-2* Generalized Anxiety Disorder-2

Table 5 Stepwise multiple regression analysis

Model	*R*	R^2	Sig	Predictors
1	0.654	0.428	< 0.001	CSI score
2	0.677	0.458	< 0.001	CSI score, PCS

Dependent variable: HRQoL (EQ-5D)

EQ-5D EuroQol 5-dimension, *CSI* Central Sensitization Inventory, *PCS* Pain Catastrophizing Scale

(all, $p < 0.001$, Table 4). In the stepwise multiple regression analysis, CSI and PCS remained to be significantly associated with EQ-5D. The coefficients of the VIF test was 1.35, showing no harmful collinearity between the variables. CSI alone accounted for 43% of the variance in HRQoL (Table 5). Moreover, CSI and PCS combined accounted for up to 46% of the variance in HRQoL in breast cancer survivors.

Discussion

In this study, 45% of breast cancer participants reported persistent pain even > 1 year after surgery. The pain group scored a higher CSI than the without-pain group and healthy controls. Moreover, although the proportion of treatment-related factors such as axillary lymph node dissection, and chemotherapy was also significantly higher in the pain group than in the without-pain group, the estimated effect sizes of CSI and PCS were larger than those of the treatment-related factors. These results suggest that CS and pain catastrophizing may be associated with the development and/or maintenance of persistent pain more than treatment-related factors.

A higher CSI score was found only in breast cancer patients with persistent pain, and the scores of CSI and psychological measurements in patients without pain were quite similar to those of healthy controls. These results strengthen our proposition that persistent pain in breast cancer patients is induced and maintained by CS. A previous study showed that although the level of anxiety and depression of breast cancer survivors decreased over time after treatment, a significant number of women had elevated anxiety and depression at 18 months of follow-up, and the anxiety at this stage was predicted by pain [34]. Therefore, higher scores of PHQ-2 and GAD-2 in our patients with pain may be developed and maintained by persistent pain, and our patients without pain may show lower anxiety and depression scores. It has been also considered that nerve damage from surgery and dermatitis radiotherapy causes persistent pain [5–7]. However, our results showed that the estimated effect sizes of CSI and PCS were larger than those of the treatment-related factors. Because the breast cancer participants in this cohort underwent surgery about 1.6 years ago, peripheral damage caused by breast cancer treatments should have been improved over time; thus, CS and pain catastrophizing may influence persistent pain at this stage. As this study was cross-sectional, it was not able to clarify whether CS and pain catastrophizing are involved in the development and/or maintenance of chronic pain. CS may have been already established before surgery, especially in people with a higher CSI score after surgery. Therefore, it is necessary to evaluate CSI before and immediately after surgery.

The EQ-5D score in the pain group was significantly lower than those in the without-pain group and healthy controls. This is consistent with the results of a previous study [25]. Hsu et al. reported that several domains of QoL in breast cancer survivors were improved over time and that these people appeared to have similar QoL in most aspects to age-matched non-cancer controls at 1 year after diagnosis [35]. Moreover, current studies have demonstrated that chronic pain resulted in lower QoL in people with breast cancer as well as other diseases [7, 36]. Improvement in HRQoL has been considered as one of the most crucial goals of cancer treatment [37]. Therefore, management of HRQoL in breast cancer survivors with chronic pain is essential in clinical practice. In our study, the multiple regression analysis demonstrated that CS-related symptoms and pain catastrophizing were associated with HRQoL more than other psychosocial factors. An increasing number of studies have shown that CSI and PCS were associated with lower HRQoL in patients with various chronic pain conditions [19, 20, 38, 39]. Our results expand these findings and indicate that the evaluation of CS-related symptoms and pain catastrophizing is important in the management of HRQoL in breast cancer survivors. Pain catastrophizing may be even stronger in breast cancer with pain because for most breast cancer survivors, recurrence or metastasis of cancer represents a serious threat [40]. Therefore, breast cancer survivors who are in pain have strong pain catastrophizing, which may adversely affect HRQoL. Therefore, clinicians could easily evaluate using CSI and PCS whether CS-related symptoms and pain catastrophizing influence HRQoL.

This study has some limitations. This was a cross-sectional study at a single institute, involving a small patient cohort; thus, future work should investigate our findings in larger samples of breast cancer patients. Furthermore, we were unable to confirm a longitudinal relationship between CS and other outcomes, so it is necessary to investigate CS before and after treatment.

Conclusions

To our knowledge, this is the first study to investigate the differences between breast cancer survivors with and without chronic pain in terms of multidimensional evaluation,

including evaluation of psychosocial factors, breast cancer treatment-related factors, and CS-related symptoms. Based on the findings, CS and pain catastrophizing may affect chronic pain more strongly than treatment-related factors in breast cancer survivors. Furthermore, CSI and PCS were the main predictors of HRQoL. Therefore, CSI and PCS may help clinicians determine the cause of lower HRQoL in breast cancer survivors.

Acknowledgements We thank Hiroe Kanamori, Izumi Kameyama, Yumi Nakakura, Yasuko Tanaka, Naoko Takahashi, and Noriko Hashimoto for assistance with data collection.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Funding The authors declare no funding sources directly relevant to the study.

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