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ORIGINAL ARTICLE

Breast cancer post-surgical impact on women´s quality of life during chemotherapy treatment: A structural equation modelling approach

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Abstract

Objective: Breast cancer is an important public health problem that is increasing in incidence, being a stressor with a negative impact on women's quality of life. This study is focused on the evaluation of temporal precursors (one month before) of women's quality of life undergoing chemotherapy, considering post-surgical personal, clinical, cognitive and neuropsychophysiological factors, according to the Transactional Stress and Coping Model.

Methods: This longitudinal study included 112 patients with breast cancer. Data were collected in two different moments: before and during the adjuvant chemotherapy. Structural equation modelling was used to support a theoretically based model in which some antecedent factors impact patients' long-term quality of life through a set of mediators.

Results: The associations of breast symptoms, body image and sexual functioning with psychological distress and quality of life were totally mediated by illness perceptions, while the associations of working memory with psychological distress and quality of life were totally mediated by self-efficacy for coping. Patients with greater psychological distress showed higher levels of nadir cortisol.

Conclusions: Results showed the importance of assessing patients' perceptions of their illness, prior to chemotherapy, as well as promoting more self-efficacy for coping, in order to improve women's emotional state and quality of life.

KEYWORDS
breast cancer, cortisol, illness perceptions, self-efficacy for coping, working memory and quality of life

1 | INTRODUCTION

Breast cancer, the most common cancer in women, is an important public health problem (Ferlay, Hery, Autier, & Sankaranarayanan, 2010). Current predictions indicate a significant rise in breast cancer in terms of incidence, but a decreasing rate of mortality perhaps due to better screening and treatment (Ferlay et al., 2013, 2018; Malvezzi et al., 2019). Breast cancer is considered a highly heterogeneous chronic disease, in its aetiological and pathological characteristics (Tao et al., 2015) with negative implications on women's quality of life (QoL) (Yan et al., 2016). The diagnosis and the course of the disease, as well as the treatment and the fear about the risk of relapse are stressful factors for patients. Behavioural or emotional reactions to stress may promote or inhibit healthy life practices and motivate or suppress health-promoting lifestyle habits (Strahler et al., 2019).

This study focuses on the Transactional Stress and Coping Model (TSCM) delineated by Lazarus and Folkman (1987), which provides a conceptual framework to understand possible mechanisms under which a set of antecedent circumstances may impact QoL over time through another set of mediating factors. TSCM is based on the interplay between four categories on a meta-theoretical basis: (a) the antecedent causal factors, which include environmental antecedents and personal background; (b) mediation processes, which include cognitive assessments and coping strategies; (c) short-term outcomes, including emotions during and soon after the situation/stressor and physiological changes; and (d) long-term adaptation outcomes, including subjective well-being, social functioning and somatic health, such as QoL (Lazarus & Folkman, 1987).

In the first category of the TSCM, the antecedent causal factors, the present study evaluated the following variables: tumour grade, disease stage, surgery type, post-surgical side effects and cognitive functioning. In fact, clinical factors, such as advanced stages, are associated with worse QoL (Filazoglu & Griva, 2008; Kwan et al., 2010). Previous studies have shown the association of surgery type on patients' body image, psychological morbidity (Rippy et al., 2014) and sexuality (Cornell et al., 2017). Surgical side effects, such as breast and arm symptoms, social function and sexual satisfaction (Bueno et al., 2018), have also been negatively associated with QoL in women with breast cancer (Collins et al., 2010). Regarding cognitive functioning, there is also evidence that it may already be impaired in pre-treatment (Hermelink et al., 2015; Menning et al., 2015), particularly the attention level and the working memory, which may become risk factors for cognitive changes after treatment (Cimprich et al., 2010), with long-term implications on QoL (Tometich et al., 2019).

In the second category of the TSCM, regarding the mediation processes, the present study included self-efficacy for coping and illness perceptions. According to the TSCM, when confronted with a stressor, the individual evaluates the situation cognitively to estimate whether the stressor is irrelevant, benign-positive or stressful (primary appraisal). Subsequently, the person assesses the capability to manage the situation for personal benefit considering the coping options (secondary appraisal) available, which is similar to self-efficacy, also described in Bandura's social cognitive theory (Bandura, 1997). Previous research showed that illness perception was a consistent predictor, over time, of psychological distress (Gibbons et al., 2016) and QoL (Ashley et al., 2015).

Self-Efficacy has a positive impact on well-being (Rottmann et al., 2010), on the adjustment process after a cancer diagnosis (Loh & Quek, 2011), on QoL and on decreasing distress (Chirico et al., 2017), even one year after diagnosis (Rottmann et al., 2010). Also, cognitive appraisal has been assumed to be a mediator of QoL in women with breast cancer (Zou et al., 2014).

In the third category of the TSCM, regarding the short-term outcomes, this study evaluated anxiety, depression, emotional distress and salivary cortisol. At the time of the diagnosis or during the treatment, women tend to present high levels of anxiety, depressive symptoms and general emotional distress, with implications on long-term QoL (Lam et al., 2012; Wittmann et al., 2017). Regarding physiological changes, there is evidence that women who are not in the early stages of breast cancer (Carlson et al., 2007) show altered cortisol patterns (Sephton et al., 2000), with repercussions in the immune system and disease progression (Antonova et al., 2011; Cash et al., 2015; Zeitzer et al., 2016). In fact, nocturnal peaks are associated with the disease progression in advanced breast cancer (Zeitzer et al., 2016).

Finally, in the fourth category of the TSCM, regarding long-term results, this study assessed QoL, which is associated, as shown previously, with several factors (e.g. personal and clinical characteristics, distress symptoms, illness perceptions and self-efficacy for coping).

Many studies have confirmed the association of several variables with QoL, in cancer patients. However, those studies have not evaluated which post-surgical factors were associated with low QoL during chemotherapy and whether this effect was direct or an indirect one. This aspect is important because it allows to understand whether the implications on QoL during chemotherapy occur only from factors inherent to the treatment, or also derive from previous effects, such as surgery. Thus, this study evaluates: (1) some post-surgical and pre-chemotherapy factors that predict QoL one month later, during the chemotherapy treatment, based on the TSCM of Lazarus and Folkman (1987); and (2) whether there were mediator effects in this relationship. Knowing these factors may help to intervene earlier on and prior to the chemotherapy treatment, mitigating their implications on long-term QoL.

2 | METHODS

2.1 | Participants

Initially, a total of 134 breast cancer patients were selected in the clinical oncology services from four hospitals in the northern region of Portugal. However, only 112 met all eligibility criteria (9 refused to participate and 13 did not meet the inclusion criteria). Data were collected between February 2017 and September 2018. Patients were invited to participate by a member of the

research team. The inclusion criteria were as follows: (a) women with T1-T2 breast cancer staging; (b) being at least 18 years old; (c) level 0-2 on the Eastern Cooperative Oncology Group (ECOG) performance Status; (d) adjuvant chemotherapy treatment; and (e) absence of psychiatric illness or cognitive deficit as reported in their medical chart.

2.2 | Procedure

After the oncology consultation, the eligible candidates who fulfilled the inclusion criteria and who accepted to participate in the study signed an informed consent. The study used a longitudinal design with two assessment moments, one month apart. Considering that a time interval, in a longitudinal study, depends on a myriad of factors (the phenomenon under study, its nature, the underlying process of change over time, the context in which the process of change occurs and the variables that influence the change, Chan, 2014), one month seems appropriate to assess the QoL construct, since after an aggressive treatment such as chemotherapy, QoL is likely to change. In this study, there were two assessments moments: T0 (baseline) and T1 (1 month later). The baseline moment corresponded to the first contact with the researcher, which occurred before chemotherapy, three weeks after surgery. At the baseline, sociodemographic, clinical (including salivary cortisol) and all psychological variables, with the exception of QoL, were collected. The second moment corresponded to the second cycle of chemotherapy (three weeks after the first cycle), and QoL was the only variable assessed. The research was approved by the Ethics Committees of the four hospitals where data collection took place (Approvals: nº11133/2016; ref.39/2017; nº9/2016; CESHB 015/2016).

2.3 | Measures/Instruments

The Cronbach´s alpha found in this study for each variable are described in Table 2.

2.3.1 | ECOG Performance Status (Oken et al., 1982)

The Zubrod scale evaluates patients' performance status, where 0 refers to fully functional and asymptomatic and 5 to dead. It was used for inclusion criteria (West & Jin, 2015).

2.3.2 | Sociodemographic and Clinical Questionnaire (SCQ) (Pereira & Pereira, 2017)

This instrument was developed specifically for this study and included 13 items to assess sociodemographic variables (age, marital status, education and occupation) and clinical variables (type of surgery, disease stage, number of planned treatment cycles, tumour grade, sentinel lymph node and molecular markers).

2.3.3 | WAIS III Subtest—Direct and Inverse Digit Span, (Weshler, 2008)

The instrument evaluates patients' working memory in clinical practice consisting of two parts: the Direct Order Digits (forward span) and the Inverse Order Digits (backward span). High scores indicate high immediate auditory memory and working memory.

2.3.4 | Quality of Life of the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30), (Aaronson et al., 1993; Pais-Ribeiro et al., 2008)

The instrument assesses health-related QoL in patients with cancer disease. The instrument consists of 30 questions, divided into 5 functional scales (physical, social, emotional, cognitive and role functioning), 3 scales of symptoms (fatigue, pain and nausea/vomiting) and a global Health and QoL scale. The questionnaire also presents 6 single-item scales, namely, dyspnoea, insomnia, appetite, constipation, diarrhoea and financial difficulties. In this study, only the global scale was used, with higher scores indicating better QoL.

2.3.5 | Supplementary Questionnaire Breast Cancer Module (QLQ-BR23), (Sprangers et al., 1996)

This instrument is intended for patients diagnosed with breast cancer, regardless of the disease stage and treatment modality. It consists of 23 questions with five multiple item scales aiming to evaluate the disease symptoms, treatment side effects, body image, sexual functioning and future perspective. In this study, only the breast symptoms, body image and sexual functioning subscales were used. High scores indicate a better body image, better sexual functioning and more breast symptoms. In the original version, the Cronbach's alphas for the subscales were .85 for breast symptoms, .85 for body image and .89 for sexual functioning.

2.3.6 | Illness Perception Questionnaire (IPQ-Brief), (Broadbent et al., 2006; Figueiras et al., 2010)

This instrument comprises 9 items that assess patients' cognitive and emotional representations of the illness. It consists of 5 items that evaluate cognitive representations (e.g. consequences, duration, personal and treatment control, and identity), plus two items that evaluate the emotional representations (concern and emotions) and one item that assesses the understanding about the disease.

Finally, there is one more item that is open-ended and asks the perceived causes of the illness (not used in the study). Higher scores indicate a more threatening illness perception.

2.3.7 | Cancer Behaviour Inventory-Brief Version (CBI-B), (Heitzmann et al., 2011)

This instrument consists of 12-item that evaluates self-efficacy for coping in cancer patients. Higher scores indicate more effective coping strategies. In the original version, the Cronbach's alpha was .84.

2.3.8 | Hospital Anxiety and Depression Scale (HADS), (Zigmond & Snaith, 1983; Pais-Ribeiro et al., 2007)

This instrument assesses depression and anxiety in patients with physical pathology and in outpatient treatment. It consists of 14 items divided into two subscales: anxiety and depression. Higher scores indicate greater psychological morbidity. Cronbach's alphas in the Portuguese version were .76 for the Anxiety subscale and .82 for the Depression Scale.

2.3.9 | Trail Making Test (TMT), (Partington & Leiter, 1949; Cavaco et al., 2013)

This instrument is composed of two parts: part A evaluates attention, visual tracking and speed of graphomotor coordination and information processing; Part B evaluates Part A functions together with the ability to switch between a set of stimuli. Lower raw indices and higher adjusted scores correspond to better cognitive performance. In this study, the scores derived from the ratio (B/A) were used to assess the executive function ability (Oosterman et al., 2010).

2.3.10 | Emotion Thermometers (ET), (Mitchell et al., 2010; Teixeira et al., 2019)

The instrument consists of five analogue-visual scales, with four domains to identify emotional complications (distress, anxiety, depression and anger) and one outcome domain (need for help). A high result indicates emotional distress. Only the global scale derived from the first four emotional domains was considered in the present study.

2.3.11 | Salivary cortisol

The collection of saliva for the evaluation of cortisol concentrations was performed using salivettes® (Starsedt). Each participant was given an envelope with three salivettes and an explanatory leaflet to collect saliva: (a) between 11-12 p.m. (the lower peak of cortisol rhythm, e.g. Chan & Debono, 2010), (b) the following day upon waking and fasting, and (c) thirty minutes after waking and fasting (highest peak cortisol rhythm). For all the samples, patients were requested to place the salivettes in the refrigerator until bringing them to the hospital. Participants were told to abstain from eating, drinking, smoking, brushing their teeth or taking medication 30 min before collection of saliva. Participants were also asked to write the exact time of collection of each sample. At T0, participants were not taking the post-surgical medication.

The procedure to assess salivary cortisol concentrations was implemented according to the protocol stipulated by IBL International (Cortisol Saliva ELISA, IBL International GMBH). In the present study, the unit of measure nmol/L and results were converted according to the formula available at IBL International: Cortisol (μg/dL) × 27.6 = nmol/L. The intra-assay coefficient of variation (CV) was below 5% (2.29%).

2.4 | Statistical analyses

All statistical analyses were conducted using R statistical environment (RStudio, version 3.6.2, R Core Team, 2019), through packages 'lavaan' (Rosseel, 2012) and 'semTools' (Jorgensen et al., 2019).

When all measures were completed, data were reduced using coarse factor scores for the main variables of this study. More precisely, all items composing a scale or a subscale were averaged in order to originate a new variable of interest in the dataset. Then, in order to characterise the sample, descriptive statistics were used (frequencies, means and standard deviations). A correlation matrix (Supplementary Material 1) was also computed to assess the relationship between patients´ variables (QoL was evaluated one month after the others). The significance level was set at $\alpha = 0.05$.

Finally, a structural equation model (SEM) was specified based on the TSCM model (Lazarus & Folkman, 1987). More specifically, each variable was classified into one of the four categories defined in the TSCM of Lazarus and Folkman (1987): causal antecedents, appraisal, immediate effects and long-term effects. After allocating each variable to each group, relationships between variables were specified based on both theoretical findings and on the correlation matrix of the variables. Before proceeding with further analysis, all continuous variables were standardised and centred. In order to avoid multicollinearity issues due to the high correlation between anxiety, depression and the emotion thermometers, a latent variable called 'psychological distress' was created using these three variables. This latent variable showed good construct reliability CR = .88 and good average variance extracted AVE = .72 (Fornell & Larcker, 1981). In order to improve both the fitting and the parsimony of the model, nonsignificant paths were then eliminated from the hypothesised model. The final theoretically based model is depicted in Figure 1.

The validity of this final model was assessed using adequate fitting indices, namely, the ratio of Chi-Square over the number of degrees of freedom (χ^2/df, ratios 3:1 or less indicate good fit), the root mean square error of approximation (RMSEA, values under 0.06

are acceptable), the standardised root mean square residual (SRMR, values less than 0.08 are good), the Tucker–Lewis Index and the Comparative Fit Index (TLI and CFI, respectively, values greater than 0.95 reflect a good fit) (e.g. Hu & Bentler, 1999).

The Pearson's correlations between the variables of interest and the model estimates were obtained through the package 'lavaan' (Rosseel, 2012), using a robust maximum likelihood estimator (MLR), which produced standard errors and a test statistic that are robust against non-normality. SEM tools were also used to test the main mediating effects included in the model.

3 | RESULTS

3.1 | Participants

Participants were 112 women of whom 70.5% (n = 79) did not present any comorbidity and the remaining showed: hypertension (n = 16; 14.3%); rheumatoid arthritis (n = 1; 0.9%); diabetes (n = 5; 3.6%); hypertension and dyslipidaemia (n = 4; 3.6%); glaucoma (n = 1; 0.9%); diabetes and dyslipidaemia (n = 1; 0.9%); dyslipidaemia (n = 3; 2.7%); hypertension and diabetes (n = 3; 2.7%). Tables 1 and 2 summarise the characteristics of the sample. In Table 1, the number of chemotherapy/cytotoxic cycles corresponds to chemotherapy planned cycles for each patient at the beginning of the treatment. At T1, each patient had only performed 2 of the planned cycles.

3.2 | The structural equation model

The theoretically based model outlined in Figure 1 exhibits very good fit to the data (scaled/robust versions): chi-square (χ^2) = 55.38, df = 55, χ^2/df = 1.01, CFI = 0.999, TLI = 0.999, RMSEA = 0.008 with 90% upper limit = 0.060, SRMR = 0.059. All parameter estimates are presented in Table 3.

According to the final model, where all relationships were considered simultaneously, results showed that: (a) comparing women with different types of surgery, those who underwent a mastectomy showed worse body image (β = −.94, p = .001), which contributed to more threatening illness perceptions (β = −.25, p = .001); (b) higher executive function was associated with higher working memory (β = −0.33, p < .001), that was associated with higher self-efficacy for coping (β = 0.24, p = .002) and lower psychological distress (β = −0.31, p < .001); (c) patients with higher sexual functioning revealed a better body image (β = 0.18, p = .022), increased breast symptoms (β = 0.24, p = .028) which were associated with worse body image (β = −0.23, p = .014), higher levels of working memory (β = 0.30, p < .001) and more threatening illness perceptions (β = .22, p = .002); (d) sexual functioning

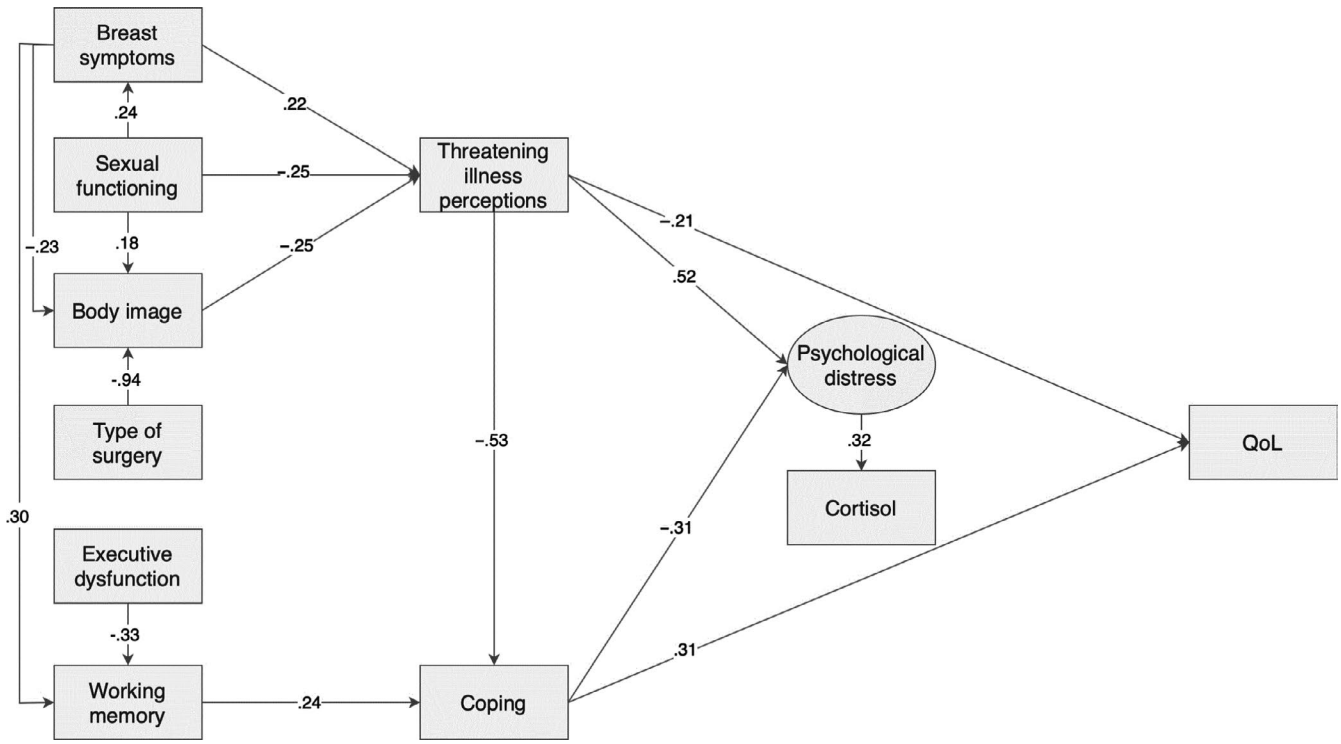

FIGURE 1 Graphical representation of the theoretically based structural equation model, based on the conceptual model from Lazarus and Folkman (1987). This model has only significant paths, which are represented by solid arrows. For simplicity, the three indicators (depression, anxiety and emotion thermometers) used to define the latent variable *Psychological distress* are not shown in this figure. Moreover, each endogenous variable is associated with an error but, for simplicity, these errors are also omitted. Detailed information about this model is presented in Table 3. Model fit indices: χ^2 = 55.38; df = 55; χ^2/df = 1.01; CFI = 0.999; TLI = 0.999; RMSEA = 0.008 with 90% upper limit = 0.060; SRMR = 0.059.

TABLE 1 Sociodemographic and clinical characteristics of BC patients (N = 112)

		Patients
		n (%) / M ± SD
Age		52.67 ± 10.29 Min (27)/Max (73)
Age group	≤45	33 (29.5)
	46-53	28 (25.0)
	54-62	26 (23.2)
	≥73	25 (22.3)
Marital status	Single	11 (9.8)
	Married/ Common law marriage	87 (77.7)
	Divorced	8 (7.1)
	Widow	6 (5.4)
Professional Situation	Employed	4 (3.6)
	Sick leave	69 (61.6)
	Unemployed	8 (7.1)
	Retired	22 (19.6)
	Domestic	9 (8.0)
Education	≤Primary studies	73 (65.2)
	≤Secondary studies	22 (19.6)
	≤University degree	17 (15.2)
Breast Cancer Grade	I	12 (10.7)
	II	73 (65.2)
	III	27 (24.1)
Cancer Stage[a]	T1	44 (39.3)
	T2	68 (60.7)
Type of Surgery	Breast conserving	90 (80.4)
	Mastectomy[b]	22 (19.6)
Number of Chemotherapy Cycles/ Cytotoxic Drugs[c]	4 cycles (AC)	37 (33.0)
	6 cycles (FEC-D)	24 (21.4)
	8 cycles (AC-D)	11 (9.8)
	16 cycles (AC-P)	40 (35.7)
Sentinel lymph node	Positive	52 (46.4)
	Negative	60 (53.6)
Molecular markers	Luminal A	6 (5.4)
	Luminal B HER2 negative	55 (49.1)
	Luminal B HER2 positive	32 (28.6)
	HER2 positive	8 (7.1)
	Triple Negative	11(9.8)

Abbreviations: BC, Breast Cancer; Min, Minimum; Max, Maximum.

[a]The TNM (T—tumour size; N—lymph node status and M—distant metastasis) classification for staging of Breast Cancer.

[b]Include modified radical mastectomy, single mastectomy and bilateral mastectomy.

[c]AC: Adriamycin-Cyclophosphamide (AC); FEC-D: 5-fluorouracil/ epirubicin/cyclophosphamide followed by Docetaxel; AC-D: Adriamycin-Cyclophosphamide followed by Docetaxel; AC-P—Adriamycin-Cyclophosphamide followed by Paclitaxel.

contributed to less threatening illness perceptions (β = −.25, p = .001); (e) women with more threatening illness perception showed lower self-efficacy for coping (β = −0.53, p < .001) and higher psychological distress (β = 0.52, p < .001); (e) patients with greater psychological distress showed higher levels of nadir cortisol (β = 0.32, p = .043); and (f) threatening illness perceptions were negatively associated with long-term QoL (β = −.21, p = .015) and self-efficacy for coping was positively associated with long-term QoL (β = .31, p = .003).

3.3 | Mediator Effects

As summarised in Figure 2 and Supplementary Material 2, the results showed that threatening illness perceptions mediated the relationship between (a) breast symptoms and psychological distress, (b) sexual functioning and psychological distress and (c) body image and psychological distress. Indeed, significant indirect effects were found in each case. In the second mediation model, the direct and the indirect effects have opposite signs indicating that the mediator is a suppressor. Although the direct effect was not significant, both the total and the indirect effects were significant. Self-Efficacy for coping was a mediator in the relationship between working memory and psychological distress. In the third model, the threatening illness perception mediated the relationship between: (a) breast symptoms and QoL, (b) sexual functioning and QoL and (c) body image and QoL. Finally, in the fourth model, self-efficacy for coping was a full mediator in the relationship between working memory and QoL.

4 | DISCUSSION

This study focused on the evaluation of post-surgical factors (assessed before chemotherapy treatment) that showed a significant association with long-term QoL, during chemotherapy treatment, based on the TSCM of Lazarus and Folkman (1987). The results showed that the side effects of surgery, such as body image, sexual functioning and breast symptoms, were associated with psychological distress and with QoL one month later. This association was mediated through women's illness perceptions. In fact, and considering illness perceptions towards breast cancer, one understands why more breast symptoms, worse sexual functioning and worse body image translated into a greater perception of the consequences and cancer symptoms of with all the associated emotional implications (McCorry et al., 2013; Rozema et al., 2009). As previously addressed, identity, consequences and emotional representations were associated with psychological distress and QoL (Ashley et al., 2015; Richardson et al., 2016). In this context, illness perceptions played a precursor role in the association between the effects of surgery, patients' psychological distress, and QoL. Threatening illness perceptions have been related to poor mental health or high levels of psychological distress (Gibbons et al., 2016; McCorry et al., 2013). The way patients assess and perceive their illness is associated with

TABLE 2 Descriptive Statistics for Clinical, Cognitive and Psychological Variables (N = 112)

Variables	Mean	Standard Deviation	Minimum	Maximum	α Alpha
Breast Symptoms	16.00	19.83	0.00	100.00	.82
Body Image	91.89	14.69	41.67	100.00	.94
Arm Symptoms	18.45	19.82	0.00	77.77	.65
Sexual Functioning	23.96	22.01	0.00	100.00	.90
Executive Dysfunction	2.68	0.88	0.00	4.90	
Working Memory	4.84	2.18	2.00	12.00	
Illness Perceptions	4.92	1.68	0.00	8.83	.69
Self-Efficacy for Coping	98.62	14.71	59.00	126.00	.91
Depression	3.36	2.90	0.00	15.00	.91
Anxiety	7.20	4.05	0.00	16.00	.88
Emotion Thermometers	17.98	12.14	0.00	40.00	.87
Salivary Cortisol Nadir	1.40	1.69	0.00	9.63	
Quality of Life	72.90	17.06	20.00	79.33	.91

Continuous variables that entered the final model. The subscale arm symptoms was not included in this study due to the low internal consistency (Cronbach's alpha was .65).

TABLE 3 Parameter estimation of Model 1, outlined in Figure 1 (n = 112)

	Estimate (β)	SE	*p-value*	95% CI
Latent Variable 'Psychological Distress'				
Anxiety	1.000	N.A.	N.A.	N.A.
Depression	.849	0.095	< .001 ***	[.663, 1.034]
Emotion Thermometers	.883	0.057	< .001 ***	[.771, .995]
Regressions				
Executive→Memory	−.333	0.073	< .001 ***	[−.477, −.189]
Breast.→Memory	.297	0.084	< .001 ***	[.131, .462]
Sexual→Breast	.235	0.107	.028 *	[.025, .445]
Memory→Coping	.241	0.078	.002 **	[.088, .393]
Perception→Coping	−.528	0.084	< .001 ***	[−.692, −.364]
Body→Perception	−.245	0.074	.001 **	[−.390, −.100]
Sexual→Perception	−.250	0.072	.001 **	[−.392, −.109]
Breast→Perception	.222	0.071	.002 **	[.084, .360]
Type Surgery→Body	−.935	0.282	.001 **	[−1.488, −.381]
Breast→Body	−.233	0.095	.014 *	[−.419, −.047]
Sexual→Body	.180	0.079	.022 *	[.025, .334]
Coping→Psychological Distress	−.313	0.083	< .001 ***	[−.475, −.151]
Perception→Psychological Distress	.515	0.073	< .001***	[.372, .658]
Perception→QoL	−.214	0.088	.015*	[−.387, −.041]
Coping→QoL	.305	0.102	.003**	[.106, .505]
Psychological Distress→Cortisol	.315	0.156	.043*	[.010, .621]

Significance: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

95% CI, 95% confidence interval; N.A., not applicable; SE, Standard error.

their physical and psychological health (Rozema et al., 2009). The literature has shown that illness perceptions are an important mediator between the illness and patients' well-being, in several chronic diseases (e.g. De Gucht, 2015; Zhang et al., 2016).

The results also revealed that higher executive dysfunction was associated with lower working memory and that the latter was indirectly related to psychological distress and QoL through the self-efficacy for coping. After surgery, women may already show cognitive

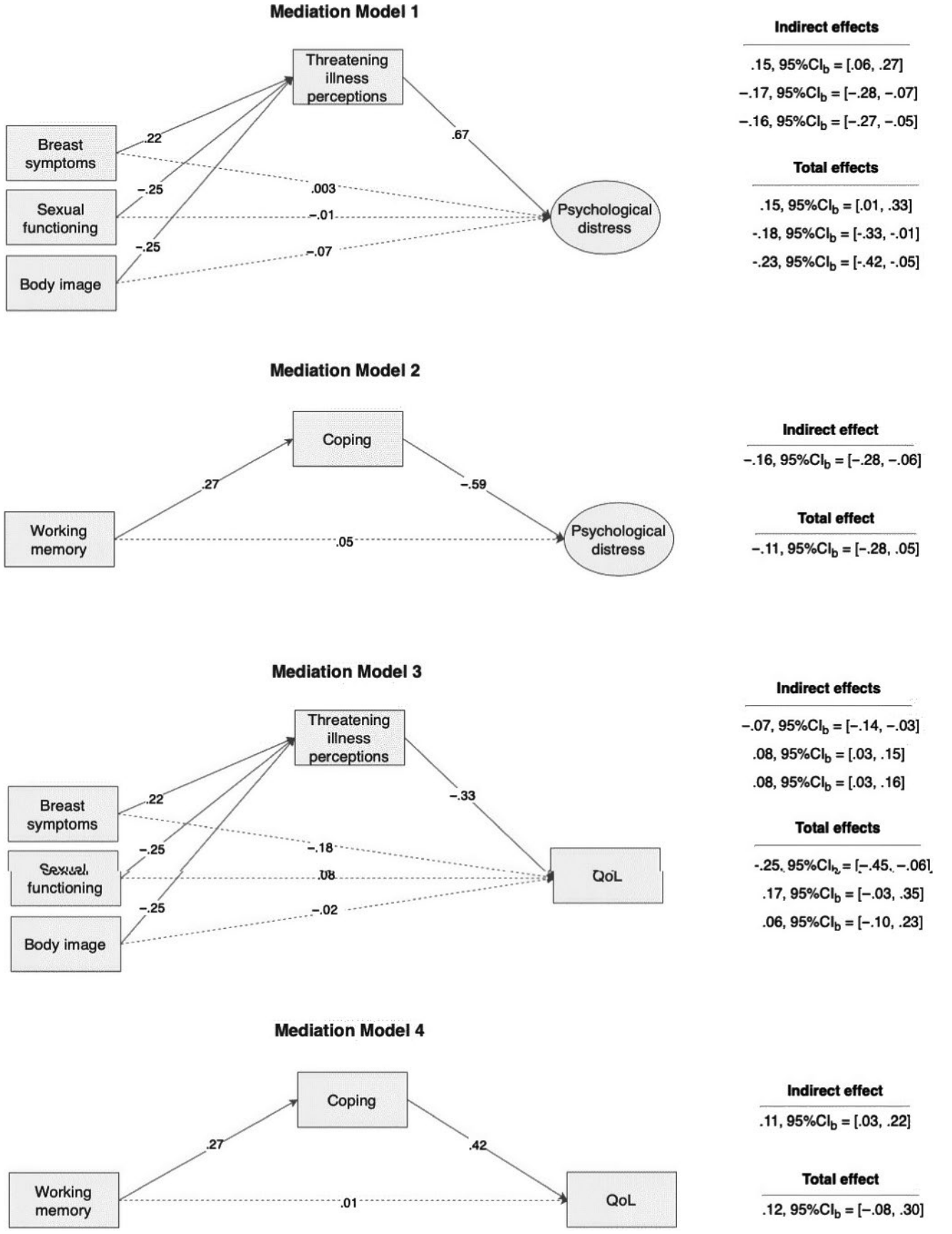

FIGURE 2 The mediator effects of self-efficacy for coping and of threatening illness perception in the structural equation model depicted in Figure 1. The total effect is the sum of the direct and indirect effects. Solid and dashed lines represent significant and nonsignificant paths, respectively. Detailed information about latent variable ('Psychological Distress') is presented in Supplementary Material 2.

changes, especially in working memory (Cimprich et al., 2010). Executive functioning encompasses a panoply of functions in which working memory is included (McCabe et al., 2010). Also, working memory is related to self-efficacy for coping, and this result may be explained taking into consideration that functional attention and working memory are prerequisites for higher cognitive functions, such as reading, decision-making and problem solving (McCabe et al., 2010). Therefore, women with better working memory are better at decision-making and problem-solving tasks, through self-efficacy for coping, which may enable the mobilisation of personal and environmental resources minimising the negative effect of the disease. Self-efficacy for coping was a precursor of psychological distress and QoL. Thus, as mentioned in the theoretical framework, individual's perceptions of their illness or stressful experience (first appraisal) influence the secondary appraisal of resources and control over the situation (Bigatti et al., 2012), determining coping strategies (Lazarus & Folkman, 1987), with emotional implications (Gibbons et al., 2016) as well as implications on QoL (Johansson et al., 2018). Therefore, the two appraisals, in addition to their predictive role, were also mediators in the final model, which validates Lazarus and Folkman's transactional model of stress and coping (1987).

Psychological distress, in addition to being associated with cortisol, by the psychoneuroimmunology (PNI) paradigm explanation (Van Der Pompe et al., 1994), may also have long-term implications on women's QoL (Wittmann et al., 2017), as it may influence recovery from surgery, as well as the experience of symptoms during the oncoming treatment. In the final model, unlike the hypothesised one, there was no relationship between psychological distress and long-term QoL. This result may be explained by the fact that in a SEM, several relationships are being considered simultaneously. Specifically, when evaluated in isolation, psychological distress (latent variable) is a temporal predictor of QoL, but when evaluated with other variables in the model, this relationship is weakened by the strength of other relationships, namely, between illness perception -> QoL and coping ->QoL. Likewise, in the final model, no direct relationship was found between cortisol and QoL, as one might have expected (although the literature is scarce) (Armer et al., 2018; Carlson et al., 2004). Probably, the time between baseline and T1 (1 month later) was not enough to establish this relationship, since it requires a change in the immunological, endocrine and cardiovascular systems that may need more time to manifest (Van Der Pompe et al., 1994). However, future longitudinal studies with assessment moments involving a longer period of time will be necessary to analyse whether this relationship persists (or not) in a consistent way, over time.

There are some limitations in this study that need to be acknowledged: (a) the majority of the instruments were self-report; (b) the sample consisted of women with breast cancer undergoing chemotherapy treatment with different cytostatics (anthracyclines and taxanes); (c) the presence of physical comorbidities (e.g. diabetes, hypertension, rheumatoid arthritis) and their psychological impact as well as cortisol effects; (d) as a result of the inclusion criteria, there may be a natural bias as the sample includes women with better medical conditions (e.g. T1 and T2 stage disease) and possibly in better psychological conditions; e) QoL was not assessed at baseline and therefore was not controlled at T0. Moreover, cortisol was evaluated only once, not providing consistency to the results that were found. Future studies should assess cortisol at least three times in consecutive days, using the same schedule at the same time, in order to assess the possible deterioration in the HPA axis and to analyse the longitudinal relationship between psychological distress/cortisol and QoL.

In conclusion, the results showed that: (a) the initial diagnosis and surgery can be a highly stressful experience for women with breast cancer due to surgery side effects and the impaired cognitive functioning that may result from it; (b) surgery side effects and impaired cognitive functioning may contribute to a (more or less) threatening illness perception; however, self-efficacy for coping may mitigate the association of side effects and cognitive functioning on patients' daily routine (personal, family and marital); (c) this stressful experience, mediated by illness perception and self-efficacy for coping, significantly influenced the risk of psychological distress and QoL at long term; (4) the results reinforce the need for psychosocial interventions in breast cancer (e.g. Andersen et al., 2008; Carlson et al., 2015; Von Ah et al., 2012) that should focus (a) on illness perceptions; (b) on self-efficacy for coping, to reduce the association with surgical side effects; and (c) on cognitive functioning, in order to decrease psychological distress and improve long-term QoL.

4.1 | Considerations about the sample size

Adequate sample size in SEM is not a straightforward question. Primary research on this topic recommended minimum values (Boomsma, 1982) and simple rules-of-thumb (e.g. Bentler & Chou, 1987; Nunnally, 1967). However, more recent studies have shown that this question is highly complex, depending on key model properties such as number of indicators and factors, the magnitude of factor loadings and path coefficients, and amount of missing data (Wolf et al., 2013). Since the sample size of this study (N = 112) may be considered small, the authors would like to make some clarifications regarding this issue. Indeed, small samples can be problematic because they influence model fit statistics and the accuracy of the parameter estimates.

Regarding model fit statistics, it is important to emphasise that there are several goodness-of-fit indices aimed at assessing the fit of structural equation models. Most of the indices depend on the sample size, usually underestimating fit when samples are small. In general, studies show that although CFI, TLI, RMSEA, SRMR favour large sample sizes, they have been found to be the most insensitive to sample size, model misspecification and parameter estimates (Hooper et al., 2008). For these reasons, these indices were used to evaluate the fit of the theoretically based model. The results indicate a very good fit.

Regarding the accuracy of parameter estimates, the problem of small samples is that they are related to inflated standard errors and, as a result, to low statistical power. Therefore, small samples limit analyses to detect large effects, a fact that strengths the significant results obtained with small samples (Combs, 2010). It is possible that nonsignificant results, in studies involving small sample sizes, would

attain significance with bigger samples. One may hypothesise that with a large sample, there would be a significant relationship between cortisol concentrations and long-term QoL.

Finally, in addition to these arguments, Bayesian arguments have also been supplied. Bayesian statistical methods were performed to assess the final model and they confirmed all frequentist results presented in this paper: parameter estimates, significance and good fitting. More precisely, using the 'blavaan' R package (Merkle & Rosseel, 2018) with defaults 10000 samples after 5000 adapt/burnin iterations, we obtained very good fitting indices: PPP = .597, BRMSEA = .005, BGammaHat = .999, adjBGammaHat = .997, Bmc = .995. Moreover, the Gelman-Rubin PSRF (potential scale reduction factor) of each parameter estimate was very close to 1, showing the efficient convergence of the model. These results are shown in Supplementary Material 3.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

COMPLIANCE WITH ETHICAL STANDARDS

Human participants and/or animal rights: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participants who agreed to participate in this study voluntarily signed an informed consent.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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