

EMOTIONAL DISTRESS AMONG LONG-TERM BREAST CANCER SURVIVORS: THE ROLE OF INSOMNIA AND WORRY

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Abstract

Breast cancer constitutes a challenge for survival and wellbeing. Emotional distress may persist many years after cancer being cured. This study aimed to analyse how emotional symptomatology was present in breast cancer survivors. Additionally, it aimed to study the role of sleep difficulty and worry on symptom maintenance. A sample of 206 women ($M= 56.07$ years, $SD= 11.56$) was selected to form four groups: healthy controls, breast cancer patients, short-term and long-term survivors. Emotional distress, worry and sleep problems were assessed. Long-term survivors showed significantly higher levels of anxiety ($p < .05$). Anxiety was predicted by worry for all groups but with higher variance in long-term survivors ($R^2_{adj} = .47$). Insomnia and age predicted depression in this group ($R^2_{adj} = .40$). To conclude, long-term emotional distress was observed even after the threat of cancer passed. Our findings confirm the need to extend supportive care to meet survivors' needs.

KEY WORDS: *anxiety, breast cancer, survivor, depression, sleep, pathological worry.*

Resumen

El cáncer de mama constituye un desafío para la supervivencia y el bienestar personal, observándose síntomas emocionales derivados que podrían persistir incluso muchos años después de superar la enfermedad. En este estudio se pretendía evaluar la presencia de sintomatología emocional en supervivientes de cáncer de mama (SCM). Asimismo, se perseguía evaluar el papel de los problemas de sueño y la preocupación en el mantenimiento de dichos síntomas emocionales. La muestra consistió en 206 mujeres ($M= 56,07$ años; $DT= 11,56$), pertenecientes a cuatro grupos: controles sanas, pacientes, SCM a corto plazo (SCMC) y SCM a largo plazo (SCML). Como resultados, se observó que los SCML mostraban más sintomatología ansiosa que los otros grupos ($p < 0,05$). Dicha sintomatología fue predicha en todos los grupos por la preocupación patológica, encontrándose mayor varianza explicada para el grupo de SCML ($R^2_{aj} = 0,47$). La edad y el insomnio predijeron la sintomatología depresiva en este grupo ($R^2_{aj} = 0,40$). Como conclusión, se debe extender la atención psicooncológica a supervivientes de larga duración dado su impacto emocional duradero.

PALABRAS CLAVE: *ansiedad, cáncer de mama, supervivientes, depresión, sueño, preocupación.*

Introduction

Breast cancer, in addition to being a life-threatening disease, also involves a compelling challenge to the individual's wellbeing and psychosocial adjustment. This ordeal begins with diagnosis, although it can last long after remission. Therefore, it is not surprising to find high levels of emotional distress and exacerbated psychological symptomatology among cancer patients (e.g., anxiety or depression), which in turn affects the patient's quality of life and daily functioning (Cheng et al., 2012; Cohee et al., 2017; Ho, So, Leung, Lai, & Chan, 2013; Zhu, Sjolander, Fall, & Valdimarsdottir, 2018). Psychosocial interventions have been extensively applied to ameliorate emotional symptomatology of breast cancer patients (Cerezo, Ortiz-Tallo, Cardenal & de la Torre-Luque, 2014; Cousson-Gelie, Bruchon-Schweitzer, Atzeni, & Houede, 2011).

After treatments and remission, the next step is to adjust to daily life after the disease. However, this adjustment may prove to be quite difficult, as survivors must live with varying sequelae derived from medical treatments and the disease, such as physical and/or psychological (Cesario, Nelson, Broxson, & Cesario, 2010; Ehrhardt et al., 2018; Kibar, Aras, & Dilialioglu, 2017; Roiland & Heidrich, 2011). Additionally, they may also have experienced a reduction or loss of income, a loss of functionality, and/or disability. The impact of these circumstances on breast cancer survivors (BCS) has led some researchers to consider cancer as a chronic stressor, with effects observed even many years after the disease remitted (Naus, Ishler, Parrott, & Kovacs, 2009; Stein, Syrjala, & Andrykowski, 2008).

BCS have complained about significant emotional distress across survivorship (Cheng, Sit, & So, 2016; Harrington, Hansen, Moskowitz, Todd, & Feuerstein, 2010; Lo, Yates, & Chan, 2018; Molassiotis et al., 2017; Smith et al., 2018). Wang et al. (2014) showed greater levels of anxiety and depression in BCS than in the healthy controls. It has also been shown that the prevalence rates of distressing symptomatology are 20-30% among survivors (Knobf, 2011).

Many factors may influence the onset and maintenance of anxiety and depression across survivorship. From a behavioural perspective, the practice of worrying as a generalised and maladaptive coping strategy should be considered. Worry is usually present in some anxiety disorders (i.e., generalised anxiety disorder [GAD]) but not exclusively, due to its distinctive features as a maladaptive coping strategy. In this regard, not only GAD patients show high levels of worry (Kertz, Bigda-Peyton, Rosmarin, & Bjorgvinsson, 2012; Ruscio & Borkovec, 2004). Moreover, worry is associated with emotional regulation impairments (e.g., lack of awareness in emotional experiences, alterations in emotional cue processing), even when a mental disorder is not present (Oathes, Siegle, & Ray, 2011; Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006). In line with Nolen-Hoeksema, Wisco and Lyubomirsky (2008) worry is a repetitive, perseverative and self-focused form of thought involved in dealing with threats that might occur in the future.

Worrying may entail an attempt to address the amount of concerns that a cancer survivor has to deal with, and which in turn could boost emotional symptomatology (Borkovec, Ray, & Stober, 1998; Bresner et al., 2015; Schmidt et al., 2018; Watkins, 2008). Inflammatory processes (e.g., interleukin releasing) may moderate the relationship between worry and emotional symptom emergence or exacerbation, due to the hypothalamus-pituitary-adrenal axis involvement (Auer, Calvi, Jordan, Schrader, & Byrd-Craven, 2018; Segerstrom, Glover, Craske, & Fahey, 1999). Indeed, some researches have reported high levels of worry-related strategies among survivors, especially in long-term survivors (Boyes, Girgis, & Zucca, 2009; Deimlig et al., 2006).

Secondly, and from a biological perspective, the difficulty in sleeping should be mentioned on account of its repercussion on quality of life and the mental symptomatology burden (see Luyster, Strollo, Zee, & Walsh, 2012). Inflammatory processes have been linked with a cluster of symptoms which include insomnia and depression, symptoms commonly reported by cancer survivors, especially for long-term survivors (Cheng et al., 2016; Harrington et al., 2010). Moreover, it has been proposed that sleep disturbance may accentuate a depressive mood and a recurrence of depression among cancer survivors by mediation of the inflammatory processes (Daniel et al., 2016; Forsythe, Helzlsouer, MacDonald, & Gallicchio, 2012; Irwin, Olmstead, Ganz, & Haque, 2013; Otte, Carpenter, Russell, Bigatti, & Champion, 2010).

This comparative research aimed to study the presence of emotional symptomatology in patients under treatment for a breast cancer and survivors. As a result, we decided to explore how anxious and depressive symptomatology were present among BCS as well as worry as a coping strategy and sleep difficulties. Therefore, it was hypothesised that long-term BCS would show higher anxious and depressive symptomatology than individuals in other stages over the course of the disease (patients or short-term survivors) or healthy women. Moreover, it was expected that long-term survivors would exhibit higher levels of worry than the healthy women, cancer patients and short-term survivors; and higher insomniac symptomatology than the healthy women and cancer patients, but not more than short-term survivors. Secondly, our aim was to determine how insomnia and worry might predict anxious and depressive symptomatology over the disease course. We expected that worry would play a significant role on anxious and depressive symptomatology, especially for long-term survivors; conversely, insomnia-related difficulties should only show a significant influence on depressive symptomatology.

Method

Participants

A sample of 206 Spanish adult women ($M= 56.07$ years, $SD= 11.56$) were recruited. Four groups were made: the first one, made up of patients under breast cancer treatment (PCT), who were awaiting for starting a radiotherapy or chemotherapy treatment; a second group made up of short-term breast cancer survivors (STCS), those who were cancer-free and had been diagnosed with a

breast cancer at maximum five years before this study; and a group of long-term breast cancer survivors (LTCS), who had been diagnosed with a breast cancer more than five years before this study (Table 1).

Table 1
Sociodemographic and medical features of the study groups

Variables	Study groups				Contrast test	Effect size
	CG	PCT	STCS	LTCS		
<i>N</i>	48	38	85	35		
Age (<i>M</i> and <i>SD</i>)	54.89 (12.14)	57.30 (11.95)	55.20 (11.79)	57.77 (9.90)	0.70	.01
Marital status					16.31	.30
Single	22.73	18.43	17.28	2.94		
Married	68.17	71.05	70.37	64.70		
Divorced	9.10	2.63	8.65	14.71		
Widowed	0	7.89	3.70	17.65		
Employment status					4.75	.16
Employed	46.43	64.86	43.90	47.06		
Unemployed	7.14	2.70	4.88	5.88		
Retired	10.71	29.72	18.29	20.59		
Never worked	35.72	29.72	32.93	26.47		
Chronic disease	37.50	52.94	52.94	52	3.11	.14
Psychoactive medication	18.75	26.31	27.06	40	4.64	.15
Cancer stage					29.78**	.47
I	--	59.46	28.57	0		
II	--	24.32	44.16	68.18		
III	--	8.11	24.67	31.82		
IV	--	8.11	2.60	0		
Months since diagnosis	--	--	24.70 (25.62) [Range: 10.55-56.71]	118.63 (65.65) [Range: 61.72-224.30]	62.51	.52
Oncologic treatments [†]						
Chemotherapy	--	43.24	75.31	84.37	16.61**	.33
Radiotherapy	--	91.89	92.60	78.12	5.38	.19
Hormonal therapy	--	--	90.12	90.62	0.93	.01

Notes: CG= Healthy control group; PCT= Patients under cancer treatment; STCS= Short-term cancer survivors; LTCS= Long-term cancer survivors; df= degrees of freedom. Data are displayed by means and standard deviations (between brackets) for age and months since diagnosis, and as percentage of cases for categorical variable. Contrast tests were based on between-group *F* statistic for quantitative variables and on χ^2 statistic for categorical data. Effect size estimates displayed are the η^2_{partial} for quantitative variables and the Cramer's ϕ for the categorical variable. [†]All the participants in the PCT, STCS and LTCS groups underwent a surgical intervention for the breast cancer. **p*< .05; ***p*< .01.

STCS and LTCS were made according to Leigh's criteria (Leigh, 1996). All of these participants had to have been able to write, understand and read Spanish, and have handed in a written consent to participate into this study. The exclusion criteria were: being diagnosed with a sensory processing disorder or a neurodegenerative disease; being diagnosed with any terminal disease; or being suffered from cancer relapse throughout survivorship (just for cancer survivors). The fourth group (control group, CG) was composed of an age-matched sample of Spanish women without a history of cancer. They were fluent in Spanish and provided a written consent to participate.

Instruments

- a. *Hospital Anxiety and Depression Scale* (HADS; Zigmond & Snaith, 1983), Spanish version by Caro and Ibañez (1992). A 14-item instrument to measure emotional distress on a 4-point Likert scale. From the HADS, two types of symptoms can be explored: anxiety and depressive symptomatology. Thus, a score for both types of symptoms can be derived as well as a composite score of emotional distress, pointing to higher symptoms with higher scores. Psychometric properties of the scale are quite good in Spanish population, observing Cronbach's α scores from .84 to .90 (Herrero et al., 2003). Moreover, reliability indexes were shown to be adequate for the HADS factors within our sample ($.80 < \alpha < .87$, for the factors).
- b. *Oviedo Sleep Questionnaire, self-reported version* (OSQ; Bobes et al., 2000; Lopez, de la Torre-Luque, Lazo, Alvarez, & Buena-Casal, 2016). A 15-item instrument to evaluate the perceived sleep quality and the presence of sleep problems over the last month. The OSQ allows exploring varying types of sleep-related problems on a 5-point Likert scale: insomniac symptoms, hypersomnia-related symptoms, other problems related to sleep (e.g., snoring, restless legs while sleeping, etc.) and the use of aids to manage sleep difficulty (e.g., pills, lemon balm). Due to study purposes, only the index of sleep satisfaction (relied on a 7-point scale, from 1 ("very unsatisfied") to 7 ("very satisfied"), the scales of Insomnia and Hypersomnia (sum of symptoms for each scale, with higher severity with higher scores), and the item of sleep efficiency (SE) were used. This item allows the calculation of what percentage of time in bed is actually dedicated to sleep. Psychometric properties of the OSQ were satisfactory in Spanish population ($\alpha = .77$; Bobes et al., 2000). Satisfactory reliability indexes for the OSQ factors were also shown within our sample ($.70 < \alpha < .76$, between factors).
- c. *Penn State Worry Questionnaire* (PSWQ; Meyer, Miller, Metzger, & Borkovec, 2016), Spanish version by Sandin, Chorot, Valiente and Lostao (2009). A 15-item tool to measure worry, considered as a maladaptive (uncontrollable and generalised) tendency to engage in chains of problem-solving thoughts and images (Borkovec et al., 1998). The items are rated on a scale from 1 ("not at all typical of me") to 5 ("very typical of me"). A two-factor solution was described for the PSWQ (the factors are related to wording method) and a composite score of worry can be obtained from those factors. Cut-off points

to categorise worry tendencies are: scores between 16-39 may reflect low worry, scores between 40-59 may be distinctive of moderate Worry, and 60-80 may be indicative of high worry tendency. Taking into account that composite score, we found a reliability index of $\alpha = .90$, within our sample, in line with psychometric properties derived in the validation in Spanish population ($\alpha = .90$; Sandin et al., 2009).

Procedure

Protocols carried out in this study were approved by the ethics committee of the University of Granada (Spain). The study was presented to the oncology department and the community charitable organisation boards across the cities of Malaga and Granada (Spain). After the medical staff of these organisations had informed the participants about the study purposes, participants completed the questionnaires in the organisation where they were recruited in the following order: HADS, OSQ, and PSWQ. Sociodemographic and medical information were taken from the records of the organizations. Control participants were approached in different neighbourhood associations in the cities of Malaga and Granada. Three participants refused to participate into the study.

Once data collection, multiple imputation protocols were conducted to handle missing data with a threshold of five iterations. None of the study participants showed a missing rate higher than 10%. As a result, six values were imputed for the HADS from a total of 206 questionnaires filled (0.21% of values imputed); 55 values were imputed for the OSQ from a total of 167 questionnaires filled (2.74% of values imputed); and 30 values for the PSWQ were imputed from a total of 163 questionnaires filled (1.15% of values imputed).

Data analysis

Sample size estimation was conducted, considering a 4-group analysis of covariance design, with $\alpha = .05$, $\beta = .80$. As a result, a sample of 179 participants should be recruited to visualize medium effect sizes ($f = .25$). This a priori estimation was conducted using G*Power 3.1.3 (Faul, Erdfelder, Lang, & Buchner, 2007).

Regarding the data analysis upon the collected data, between-group differences on sociodemographic factors were explored using *t*-tests for independent samples and χ^2 -based tests.

To analyse the differential presence of symptomatology among the study groups, analysis of covariance (ANCOVA) was used. We considered the 4-group variable as between-group factor. Moreover, age was used as covariate. Therefore, a multivariate ANCOVA (MANCOVA) was conducted for the HADS factors (anxiety and depression). Additionally, the odds ratio was calculated to show the subclinically and clinically significant levels of depression and anxiety, comparing the cancer groups with CG. Cut-off scores were taken (see Bjelland, Dahl, Haug, & Neckelmann, 2002), with ≥ 8 for subclinical symptomatology and ≥ 11 for clinical levels, for both scales.

Another MANCOVA was run for the OSQ-related variables (insomnia, hypersomnia, and sleep efficiency) and a univariate ANCOVA was conducted for the PSWQ composite score. Moreover, the between-group differences were examined for the satisfaction index with sleep from the OSQ by means of the χ^2 -based test.

To account for the second aim, some hierarchical regressions were conducted. Concretely, a regression model was performed for anxiety and another for depression within each study group. Blocks for the anxiety regressions were: (1) age, (2) worry (PSWQ composite score); and for the depression regressions: (1) age, (2) Insomnia and SE; (3) worry. Additionally, to determine whether the regression loadings of worry and sleep variables distinctly predict the anxious and depressive symptomatology across study samples, pairwise comparisons were conducted by means of *t* tests when these regression coefficients were significant (Cohen, 1989).

Statistical analyses were conducted by means of IBM SPSS v. 24 (IBM Corp., 2016).

Results

As displayed in Table 1, no significant differences between the study groups were revealed in terms of sociodemographic features, except for cancer stage and undergoing chemotherapy ($p < .01$). A higher proportion of survivors (in both survivorship groups) underwent chemotherapy in comparison to patients under treatment. The influence of these variables (cancer stage and undergoing chemotherapy) on the criteria was discarded due to a lack of correlation with emotional symptomatology.

The MANCOVA for the HADS variables showed significant between-group differences for anxiety symptomatology ($p < .04$), with the highest levels observed in the long-term survivors (Table 2). Bonferroni *post hoc* tests revealed significant differences between these levels and those from the healthy controls ($p < .05$). Additionally, a significant effect was shown for age on the anxious symptomatology, with $F(1, 199) = 10.72$, $p < .01$, $\eta^2_{\text{partial}} = .05$. Conversely, no between-group effects were visualised for the depressive symptomatology.

Odds ratios for the risk for anxious and depressive symptomatology are displayed in Table 3. Risk for anxiety increased across the cancer trajectory, specifically that patients under treatment experienced less anxiety than the post-treatment long-term survivors. However, the risk for depressive symptomatology was the highest among short-term survivors.

Analyses of the OSQ variables failed to show significant differences between the study groups (Table 2). On the other hand, the ANCOVA for the PSWQ score did visualise between-group differences ($p < .01$). *Post hoc* tests revealed significant differences between the worry levels of LTCS and those from CG participants ($p < .05$). Accordingly, the long-term survivors showed the highest levels of worry. In addition, a significant age effect was found, $F(1, 158) = 6.65$, $p < .02$; $\eta^2_{\text{partial}} = .04$.

Table 2

Scores in psychological symptomatology and sleep difficulty according to the study groups

Psychological symptomatology	Study groups				Contrast test	Effect size
	CG	PCT	STCS	LTCS		
HADS	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>		
Anxiety [†]	5.83 (3.57)	7.51 (4.63)	7.86 (4.89)	8.18 (4.63)	2.90*	0.04
Depression	3.89 (2.65)	5.22 (3.38)	4.99 (4.01)	4.70 (3.94)	1.32	0.02
OSQ						
Satisfaction with sleep	4.46 (1.30)	4.06 (1.34)	4.19 (1.60)	4.21 (1.73)	13.11	0.28
SE (%)	90.16 (14.69)	83.91 (15.63)	83.62 (16.20)	87.37 (17.19)	1.31	0.03
Insomnia	18.50 (7.28)	20.27 (6.23)	20.12 (6.81)	18.88 (6.05)	0.82	0.02
Hypersomnia	4.90 (2.49)	5.84 (3.23)	4.90 (2.54)	4.79 (2.44)	0.70	0.02
PSWQ [†]	47.42 (11.27)	48.11 (9.85)	53.75 (14.31)	55.75 (12.30)	4.98*	0.09

Notes: HADS= Hospital Anxiety and Depression Scale; OSQ= Oviedo Sleep Questionnaire; SE= Sleep efficiency; PSWQ= Penn State Worry Questionnaire; CG= Healthy control group; PCT= Patients under cancer treatment; STCS= Short-term cancer survivors; LTCS= Long-term cancer survivors. Contrast tests were based on between-group *F* statistic for quantitative variables and on χ^2 statistic for categorical data (satisfaction with sleep). Effect size estimates displayed are the η^2_{partial} for quantitative variables and the Cramer's ϕ for the categorical variable. [†]Covariate age was significant for that criterion ($p < .05$). * $p < .05$.

Table 3

Risk of subclinical and clinical symptomatology among the clinical groups

	Subclinical		Clinical	
	OR	CI 95%	OR	CI 95%
PCT				
Anxiety	2.23	(0.91, 5.48)	1.34	(0.45, 4.00)
Depression	3.11	(0.96, 10.10)	1.06	(0.98, 1.14)
STCS				
Anxiety	2.30	(1.08, 4.89)	1.75	(0.71, 4.30)
Depression	3.58	(1.27, 10.07)	1.11	(1.04, 1.20)
LTCS				
Anxiety	2.80	(1.12, 6.97)	2.88	(1.03, 8.02)
Depression	3.36	(1.03, 10.96)	1.17	(1.02, 1.34)

Note: PCT= Patients under cancer treatment; STCS= Short-term cancer survivors; LTCS= Long-term cancer survivors.

Hierarchical regressions for anxious and depressive symptomatology are displayed in Table 4. Previously, correlations between factors and criteria were explored to discard overlap between variables. As a result, correlations were lower than .70 for all cases ($r = .46, p < .05$ for HADS depression and OSQ insomnia; or $r = .63, p < .05$ for HADS depression and OSQ insomnia). Significant regression models were found to explain anxious symptomatology for each study group, revealing worry as the significant explanatory factor for all of these models. In turn, for explaining the anxious symptomatology among the long-term survivors, this model

explained the greatest percentage of criterion variance. However, no significant pairwise differences were found regarding the regression coefficient of worry for each study group. Although, the explanatory models for depressive symptomatology were more heterogeneous among groups: worry, showed a positive loading for controls, patients under medical treatment and for short-term survivors; and sleep efficiency showed a negative loading for controls and short-term survivors. No significantly different loadings were revealed between these groups for these predictors, according to the pairwise *t* tests. Interestingly, the explanatory model for the depressive symptomatology in long-term cancer survivors included age and insomnia symptomatology, both with a positive loading, as significant regression factors.

Table 4

Explanatory models for anxious and depressive symptomatology according to the study groups

Study groups/ regression parameters	Regression criterion	
	Anxiety	Depression
CG		
<i>F</i>	15.73	9.34
<i>R</i> ² adjusted	.40	.50
Factors (β)	Worry (.62)	SE (-.48), Worry (.58)
PCT		
<i>F</i>	6.05	4.06
<i>R</i> ² adjusted	.33	.33
Factors (β)	Worry (.40)	Worry (.38)
STCS		
<i>F</i>	16.20	11.17
<i>R</i> ² adjusted	.35	.47
Factors (β)	Worry (.57)	SE (-.34), Worry (.39)
LTCS		
<i>F</i>	13.04	5.66
<i>R</i> ² adjusted	.47	.40
Factors (β)	Worry (.74)	Age (.44), Insomnia (.54)

Notes: CG= Healthy control group; PCT= Patients under cancer treatment; STCS= Short-term cancer survivors; LTCS= Long-term cancer survivors; SE= Sleep efficiency. Parameters from the significant regression models to explained criterion are displayed in this table: the *F* derived from the ANOVA, the explanatory effect size of that model (*R*² adjusted), and significant factors that attached in these models (with the standardized factorial loadings, β , between brackets). All the *F* statistics were significant with $p < .05$. Moreover, all the factorial loadings were significantly different from zero ($p < .05$).

Discussion

The cumulative effects from tolerating sequelae management, fear of a cancer recurrence, and body dissatisfaction, among other concerns, can put breast cancer survivors at risk of suffering emotional distress. For this reason, cancer is increasingly being considered as a chronic stressor with adverse effects lasting many years after remission (Naus et al., 2009; Stein et al., 2008).

The aim of this study was to examine whether emotional symptomatology was present among BCS. To achieve this aim, a comparative study was conducted with healthy women, patients under breast cancer treatment and both short-term and long-term survivors. It was also of interest to study the influence of common risk factors of emotional disorders: the generalised use of worry to cope with problematic situations, as well as the sleep difficulty. Both factors have been strongly linked with depression and anxiety symptoms (Basta, Chrousos, Vela-Bueno, & Vgontzas, 2007; Ferrer, Martin-Vivar, Pineda, Sandin, & Piqueras, 2018; Luyster et al., 2012; Oginska-Bulik & Michalska, 2019). Our results revealed that long-term survivors suffered from the highest levels of anxiety and worry among the study groups and was significantly different than those from healthy controls. Moreover, we found that worry played a relevant role in predicting the anxious symptomatology found among long-term survivors.

Survivors must confront varying vicissitudes on a daily basis. As a result, a sense of uneasiness, angst, fear of recurrence and agitation may invade long-term survivors, as well as anxious symptoms. Our results highlighted that long-term survivors had a higher tendency to show anxiety symptoms than the rest of study groups. Additionally, the risk for subclinical and clinical anxiety symptomatology was the highest in long-term survivors. In other words, it would be very likely that participants from the LTCS group show meaningful levels of anxiety symptoms (on average, LTCS participants scored over the subclinical cut-off point in the HADS Anxiety scale; by contrast, participants from the CG scored below this point), much higher than those from the CG (a medium effect size of $d = .57$ endorsed how large differences between the CG and LTCS scores were).

None of the other groups (i.e., patients under treatment and short-term survivors) showed significantly different levels of anxiety, in comparison to healthy controls. Harrington et al. (2010) reported anxiety to be one of the most prevalent symptoms among long-term survivors of gynaecological cancers. In fact, the studies gathered in their review pointed to prevalence rates of over 14.60% of long-term survivors suffered from subclinical anxious syndromes. Another meta-analysis supported that long-term survivors had a tendency to show higher levels of anxiety than healthy controls, and have an increased risk of suffering an anxiety disorder from two years after treatment end (Mitchell, Ferguson, Gill, Paul, & Symonds, 2013). Moreover, our results stated that this risk may persist over the long term after becoming cancer-free. Subclinical anxiety has been associated with the development and exacerbation of multiple physical and psychological conditions (Aparicio et al., 2013; Bosman et al., 2019; Thurston, Rewak, & Kubzansky, 2013).

In a same vein, our study found that long-term survivors showed higher levels of maladaptive worry than the rest of the study groups. Regarding comparison between the CG and LTCS participants, effect size of difference was medium, $d = .71$. This means that scores from both groups differed by more than 0.70 standard deviations. Moreover, it is important to mention that it was more likely for participants from the LTCS group to show high worry (cut-off point = 60; Meyer et al., 1990) levels (53.33% of participants) in comparison to CG participants (12.76%), despite overall scores from both groups pointed to moderate worry

levels. Additionally, worry showed a significant predictive loading on anxiety symptoms across the study groups. Worry as a coping strategy may become uncontrollable, maladaptive and highly resource-consuming, leading to heightened arousal and emotional distress (Nolen-Hoeksema et al., 2008; Watkins, 2008). As a result, its influence on anxiety symptoms may become evident, regardless individual's health status. Interestingly, the highest loading of worry on anxiety symptoms was uncovered for long-term survivors. The wide variety of daily concerns that long-term survivors must deal with leads to the development of a generalised and persistent pattern of attempting to solve those concerns mentally. Many studies have reported that it is very common for long-term survivors to show high levels of worry and ruminative thoughts, especially those related to health concerns (Auer et al., 2018; Bresner et al., 2015; Deimlig, Brown, Albitz, Burant, & Mallick, 2015; Deimlig et al., 2006; Koch, Jansen, Brenner, & Arndt, 2013; Van de Wal, Servaes, Berry, Thewes, & Prins, 2018). We suggest that long-term survivors suffer from higher levels of worry because they must deal with more health-related concerns, as a consequence of adjusting to cancer survivorship, considered as a chronic condition. By contrast, main concerns for cancer patients are related to health status, treatment-related side effects and daily adjustment to new reality (e.g., new working status, new family roles and task distribution at home). Although these concerns may become less important once treatment is delivered (McCaughan, Prue, Parahoo, McIlpatrick, & McKenna, 2012). Short-term survivors may be more worried about cancer recurrence and symptom burden (Phillips et al., 2013). However, medical follow-ups are quite frequent during the five first years of survivorship (health care professionals may help survivors to deal with those concerns) and survivors may not engage in worrying so frequently.

Regarding depressive symptoms, our study did not show differences between the study groups. In other words, both the survivor groups and the patient group did not show higher levels of depressive symptoms than controls. Some studies support that long-term cancer survivors did not always show depression or at least no differently than other populations (Harrington et al., 2010; Mitchell et al., 2013; Reed et al., 2017). Likewise, some studies support that depressive symptomatology tends to decrease across survivorship (Keating, Norredam, Landrum, Huskamp, & Meara, 2005; Stafford & Judd, 2010). The findings of this study aligned with these results in the extent that the risk for showing (sub)clinical depression was the highest among short-term survivors and decreased with long-term survivorship. Life after medical treatments, coupled with the related confrontation with a new body image and the sequelae due to the cure process, as well as psychosocial factors (e.g., social support, coping style) may influence how this symptomatology evolves across survivorship (Cheng et al., 2016; Syrowatka et al., 2016).

Depressive symptoms were differently explained across the study groups. In this regard, worry and sleep efficiency was proven to be significant for depressive symptoms prediction in healthy controls and short-term survivors. Worry was found to be significant predictor of the depressive symptoms of cancer patients. Finally, insomniac symptomatology and age (the older the participant, the more severe symptomatology) were proven to be significant predictors of depressive

symptomatology for the LTCS women. Conversely, we did not observe that worry was a significant explanatory factor for long-term survivor depression, although it did for the rest of study groups. These results are in line with Boyes et al. (2009). We speculate that worry is more related to potential catastrophic events (e.g., cancer recurrence or significant loss in household income) that could occur in the future (Nolen-Hoeksema et al., 2008). As a consequence, it is more likely that anxiety feelings and hyperarousal emerge.

On the other hand, sleep difficulty and more concretely, insomniac symptomatology, was found to be a significant factor to explain depression. Consequently, higher levels of insomniac symptomatology, in addition to age, predicted higher levels of depressive symptomatology in long-term survivors. Sleep efficiency served as a significant predictor of depression in healthy controls and short-term survivors but not for cancer patients. In healthy samples, sleep disturbance has been linked with depression recurrence and is considered (especially short sleep time) to be a risk factor for cancer proliferation (Irwin et al., 2013; Luyster et al., 2012). Nonetheless, depression has been found to be highly linked to the efficacy of oncologic treatments, although it is mediated by the coping style (e.g., optimism) and social support, but not by sleep difficulty (Bortolato et al., 2017; Fiorentino, Rissling, Liu, & Ancoli-Israel, 2011).

Some studies have provided evidence to support the role of insomniac symptomatology in depressive syndromes among long-term cancer survivors (Daniel et al., 2016; Otte et al., 2010). First, sleep difficulty is a common long-term side effect of cancer and treatments (Forsythe et al., 2012). On the other hand, living with sleep problems is directly associated with depression symptom exacerbation and poor response to depression treatment (Manber & Chambers, 2009). Irwin et al. (2013) proposed that sleep disturbance may influence depressive symptomatology through the inflammatory processes, mainly by increases in proinflammatory cytokine releasing. These researchers cited some studies where the induction of sleep deprivation lead to an increased in of interleukin-6 circulation during the day with higher levels of NF- κ B activity during night, especially for women. Moreover, they suggested that the insomniac symptomatology in survivors may have a higher impact on the depressive state and the sleep process after cure, mainly because inflammation activity tends to be heightened across survivorship.

To sum up, this study aimed at shedding light on how important is to consider the emotional symptomatology as long-term effects in long-term survivorship. The findings of this study are aligned with Stein et al. (2008), in the sense that long-term effects derived from cancer may arise many years after overcoming a (breast) cancer. Basing on a comparative study, with clinical groups and healthy controls, we found that anxiety and worry were significantly higher in long-term survivors in comparison with healthy controls. Moreover, anxious symptomatology that was highly related to worry and depressive symptomatology was strongly linked with insomniac symptomatology and higher age level in this population.

This study has some limitations to be taken into consideration. First, it would have been interesting to study the patients' prior histories of depressive and

anxiety disorders. However, this study focused on current symptomatology, while further research should include survivors' history of mental symptomatology. Additionally, a more exhaustive assessment of cancer sequelae should have been recorded (e.g., lymphedema, cancer-related fatigue, among others) to examine other potential factors influencing anxiety and depression (e.g., dispositional factors, such as resilience or personality: see, for instance, Alonso-Tapia, Rodriguez-Rey, Garrido-Hernansaiz, Ruiz, & Nieto, 2019). However, we opted for analysing the effect of our study targets separately in order to discard the confounding influence of other factors. Finally, our results were taken from a cross-sectional study. Further research with longitudinal designs should be done.

This study has some implications regarding clinical assessment and treatment prescription. First, the assessment of worry and sleep difficulty deserves being incorporated into regular protocols to make a more accurate picture on clinical status of cancer patients and survivors (see Cobeanu & David, 2018). Second, it becomes crucial to provide supportive care in order to meet psychosocial long-term survivor needs. Cancer treatment does not only consist of delivering oncology treatments for tumour removal or recurrence prevention. Cancer patients may suffer from significant physical and mental symptomatology even many years after overcoming the disease. Studies like this aim at promoting a better understand of long-term survivor care needs and claiming for extending integrative care to improve quality of life and palliate the chronic effects of cancer after cure.

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