

# Active and Passive Coping Strategies

## Comparing psychological distress, cortisol, and proinflammatory cytokine levels in breast cancer survivors

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**BACKGROUND:** Breast cancer survivors can experience psychological distress, such as anxiety and depression, long after treatment has ended, and the development of such negative affective states has been related to the coping strategy used by the survivor. In addition, coping strategies can affect the immune and endocrine systems, which are linked to anxiety and depressive symptoms.

**OBJECTIVES:** This pilot study aims to determine whether different coping strategies are associated with differences in psychological distress, cortisol, and tumor necrosis factor (TNF)- $\alpha$  levels in breast cancer survivors.

**METHODS:** 54 breast cancer survivors completed the Stress Coping Questionnaire and the Hospital Anxiety and Depression Scale and provided a blood sample for cortisol and proinflammatory cytokine measures.

**FINDINGS:** Passive coping strategies were associated with higher psychological distress, cortisol, and TNF- $\alpha$  levels. The passive group had more avoidance and negative self-targeting and less positive reappraisal and focusing on a problem's solution.

### KEYWORDS

psychological distress; cortisol; tumor necrosis factor; breast cancer; coping

**BREAST CANCER IS THE MOST COMMON CANCER** in women worldwide. Although cancer survival rates have increased, survivors often face additional mental health diagnoses, such as anxiety or depression, long after treatment has ended (Bower, 2008). These disorders lead to poorer quality of life and compromise patient health outcomes (Smith, 2015). Depression is a clear predictor of reduced survival and facilitates cancer progression, likely through changes in the hypothalamic-pituitary-adrenal (HPA) axis and the immune system (Feller et al., 2019). Physiopathology of anxiety and depression is characterized by an HPA axis dysregulation and an inflammatory response (Furtado & Katzman, 2015a, 2015b; Gerritsen et al., 2019). Therefore, an important and modifiable risk factor for the development of anxiety and depressive symptoms can be the coping strategy used (Geyikci, Cakmak, Demirkol, & Uguz, 2018; Reich & Remor, 2010).

Coping styles dictate the response to threats or challenges to prevent or reduce associated distress (Ghanem et al., 2019). Categories of coping styles are active coping and passive (or avoidant) coping (Nielsen & Knardahl, 2014). Active coping is generally associated with more adaptive adjustment and characterized by strategies such as problem-focused coping, whereas passive coping is defined as maladaptive strategies when faced with stressful situations, such as negative self-targeting and avoidance (Wood & Bhatnagar, 2015). Studies suggest that coping style can determine the immune and endocrine responses to stress (Diaz, Aldridge-Gerry, & Spiegel, 2014; Hoyt et al., 2014; Tripathy, Tripathy, Gupta, & Kar, 2019). Passive coping rather than active coping has been associated with poorer immune response and flatter cortisol diurnal slope (Dougall, Wroble Biglan, Swanson, & Baum, 2012; Hoyt et al., 2014). A meta-analysis reported that positive psychological traits are associated with reduced HPA reactivity in healthy populations (Chida & Hamer, 2008) and in patients with cancer (Diaz et al., 2014).

Patients with breast cancer who exhibit psychological distress can demonstrate ineffective coping strategies, such as negation or avoidance (Alcalar, Ozkan, Kucucuk, Aslay, & Ozkan, 2012; Donovan-Kicken & Caughlin, 2011; Malik & Kiran, 2013). A problem-focused coping strategy has been associated with better psychological outcome (Büyükaşik-Çolak, Gündoğdu-Aktürk,

& Bozo, 2012). Studies suggest that the persistent elevation of cortisol usually found in these women might be related to their failure to cope with stress during breast cancer survivorship because ineffective emotion regulation may exacerbate the HPA axis, as well as immune system activity (Appleton, Buka,

**TABLE 1.**  
SAMPLE CHARACTERISTICS (N = 54)

CHARACTERISTIC	$\bar{x}$	SD
Age (years)	51.6	6.79
Time since the end of treatment (years)	4.22	1.3
Psychological distress	12.72	6.69
<b>Coping style</b>		
Focusing on a problem's solution	15.63	4.61
Negative self-targeting	6.81	3.54
Positive reappraisal	15.93	4.33
Open emotional expression	8.85	3.28
Avoidance	9.93	4.94
Seeking social support	14.31	5.31
Religion	3.67	5.35
CHARACTERISTIC	n	
<b>Marital status</b>		
Married	25	
Divorced	14	
Single	12	
Widowed	3	
<b>Education level</b>		
Secondary/tertiary or higher	27	
<b>Type of treatment<sup>a</sup></b>		
Chemotherapy	47	
Radiation therapy	37	
Mastectomy	29	
Hormonal treatment	24	

<sup>a</sup>Participants may have had more than one type of treatment.

**Note.** Coping was assessed with the Stress Coping Questionnaire, with scores ranging from 0 to 24, and with higher scores indicating a greater use of the coping style. Psychological distress was assessed with the Hospital Anxiety and Depression Scale, with scores ranging from 0 to 21, and with higher scores indicating a higher level of anxiety or depression.

Loucks, Gilman, & Kubzansky, 2013; Graham et al., 2006; Hsiao et al., 2013; Lam, Dickerson, Zoccola, & Zaldivar, 2009). Increased levels of both cortisol and the proinflammatory cytokines, such as tumor necrosis factor alpha (TNF- $\alpha$ ), have been measured in patients with cancer and depression, including patients with breast cancer (Bouchard et al., 2016; Cirulli et al., 2015; Smith, 2015). In addition, several studies support the tumor-promoting effect of TNF- $\alpha$  (Cai et al., 2017; Ham, Fernandez, D'Costa, & Brodt, 2016). Korobeinikova et al. (2015) reported that TNF- $\alpha$  308 polymorphism might modulate the risk of breast cancer recurrence and metastasis of patients with breast cancer. Master et al. (2009) reported that TNF- $\alpha$  levels in healthy people were negatively correlated with active coping. Positive associations between maladaptive coping styles and breast cancer incidence and other cancer outcomes have been reported (Svensson & Hansson, 2016; Watson, Homewood, & Haviland, 2012).

Few studies have evaluated the relationship among coping strategy, psychological distress (or anxiety and depressive symptoms), and changes in the immune and endocrine system. Depressive symptoms have been associated with passive coping and increased saliva cortisol levels (Höhne et al., 2014). Strategies such as emotional acceptance moderate the associations between cytokines and sickness symptoms in patients with breast cancer (Reed et al., 2016).

The purpose of this study is to examine whether adopting a certain coping style is associated with differences in psychological distress and physiologic variables in breast cancer survivors. The study aims included the following:

- Classify breast cancer survivors' coping strategies into two categories: active and passive.
- Compare anxiety and depressive symptoms between women who are actively or passively coping.
- Compare TNF- $\alpha$  and cortisol levels between women who are actively or passively coping.
- Study the predictive role of coping, cortisol, and TNF- $\alpha$  on psychological distress.

## Methods

The study used a cross-sectional descriptive design to determine breast cancer survivors' use of coping strategies during stressful situations and the relationship of those strategies to psychological distress, cortisol, and TNF- $\alpha$  levels.

## Sample

Fifty-four female breast cancer survivors (aged 34–64 years,  $\bar{X}$  = 51.6 years) were recruited from various cancer associations through public talks or informative letters. The inclusion criteria for this study were being aged 30–65 years, completing all active cancer treatments (surgery, chemotherapy, and/or radiation therapy), and being at least or more than one year since the end of treatment. The exclusion criteria were women with metastases and women

who presented current medical conditions or medications that would affect inflammation, such as systemic corticosteroids or chronic inflammatory disease. Any other medical treatment was allowed. Women meeting the inclusion criteria were contacted. During day 1 of contact, investigators conducted a psychological interview. During day 2 of contact, participants provided blood samples. Participants were not compensated. Prior to any data collection, informed consent was obtained in accordance with procedures approved by the Clinical Research Ethics Committee of the Basque Country and the Ethical Committee of the Basque Country University.

### Psychological and Physiologic Variables

The psychological measures used included the Stress Coping Questionnaire (SCQ) and the Hospital Anxiety and Depression Scale (HADS).

The SCQ (Sandin & Chorot, 2003) evaluates seven basic styles of coping used to face stressful situations: seeking social support (e.g., “I asked some family member or friend for advice to better cope with the problem.”) (Cronbach alpha = 0.855), open emotional expression (e.g., “I behaved in a hostile manner with others.”) (Cronbach alpha = 0.76), religion (e.g., “I prayed.”) (Cronbach alpha = 0.899), focusing on a problem’s solution (e.g., “I tried to analyze the causes of the problem to be able to cope.”) (Cronbach alpha = 0.786), avoidance (e.g., “I tried to forget everything.”) (Cronbach alpha = 0.752), negative self-targeting (e.g., “I understood that I was the main cause of the problem.”) (Cronbach alpha = 0.802), and positive reappraisal (e.g., “I tried to focus on the positive aspects of the problem.”) (Cronbach alpha = 0.713). The participants were asked to answer 42 questions on a five-point Likert-type scale ranging from 0 (never) to 4 (almost always), which generated the scores for each subscale, ranging from 0 to 24, with a higher score indicating a higher level of coping.

The HADS (Zigmond & Snaith, 1983) is used to identify psychological distress in the hospital setting. This test is divided into two subscales: anxiety and depression (Cronbach alpha = 0.801 and 0.792, respectively). The total score for each seven-question subscale is obtained on a four-point Likert-type scale, ranging from 0 to 3. This generates the total score for each subscale, which ranges from 0 to 21, with a higher score indicating a higher level of anxiety or depression. The total scores for both subscales provide the psychological distress score (Cronbach alpha = 0.845).

The blood extraction was done in rest conditions, according to common procedures, between 8 am and 10 am by a clinical nurse in a conditioned room of the Basque Country University—a time that coincides with the maximum peak of cortisol (Debono et al., 2009). The blood was collected into serum separator tubes, centrifuged for serum acquisition, and stored at  $-80^{\circ}\text{C}$ . The serum cortisol and TNF- $\alpha$  concentration was determined using a commercially available enzyme-linked immunosorbent assay (ELISA)

kit and an ELx 800 plate reader. The assay sensitivity of cortisol and TNF- $\alpha$  was 56.72 pg/ml and 0.106 pg/ml, respectively, and the intra- and inter-assay variation coefficients were 8.1%–9.3% and 5.3%–8.3%, respectively.

### Statistical Analysis

Data obtained in this study were analyzed using IBM SPSS Statistics, version 22.0. Given that some variables do not have a normal distribution, the cortisol, cytokine, anxiety, and depression levels were normalized using the Bloom transformation to

**TABLE 2.**  
ANALYSIS OF THE SCQ SUBSCALES BASED  
ON PASSIVE OR ACTIVE COPING STRATEGIES

SUBSCALE	$\bar{x}$	SEM	p
<b>Focusing on a problem’s solution</b>	15.63	0.628	< 0.001
Passive	12.95	1.161	–
Active	17.09	0.62	–
<b>Negative self-targeting</b>	6.81	0.482	< 0.001
Passive	10.05	0.585	–
Active	5.06	0.451	–
<b>Positive reappraisal</b>	15.93	0.589	< 0.05
Passive	15.02	0.979	–
Active	16.42	0.742	–
<b>Open emotional expression</b>	8.85	0.447	–
Passive	8.47	0.719	–
Active	9.06	0.574	–
<b>Avoidance</b>	9.93	0.673	< 0.01
Passive	12.95	0.867	–
Active	8.29	0.805	–
<b>Seeking social support</b>	14.31	0.723	–
Passive	13.95	1.213	–
Active	14.51	0.912	–
<b>Religion</b>	3.67	0.728	–
Passive	3.58	0.995	–
Active	3.71	0.995	–

SCQ—Stress Coping Questionnaire; SEM—standard error of measurement  
**Note.** Coping was assessed with the SCQ, with scores ranging from 0 to 24, and with higher scores indicating a greater use of the coping style.

address asymmetric distributions (Ayán & Díaz, 2008). The variables were normalized to mitigate the violation of the normality assumption to enable the subsequent parametric analyses to be carried out. To classify the women in two groups depending on the coping strategy used, the authors conducted a hierarchical cluster and multivariate discriminant analysis with the subscales obtained from the SCQ. To study the differences between two groups, psychological and physiologic variables were analyzed using multivariate analyses of covariance, taking into account the effect of age and hormonal treatment because of their impact on the biologic variables studied (Heaney, Phillips, & Carroll, 2010; To, Cheung, Lazarus, Knower, & Clyne, 2014). The relationships between the variables were examined using Pearson correlations. With the aim of analyzing the potential predictive role played by coping, cortisol, and cytokine levels, regression analyses were conducted with psychological distress as the dependent variable. To ensure the robustness of the analysis, the quantity range of subjects was estimated for each of the variables included in the regression model (Field, 2009). Finally, the

**TABLE 3.**  
DIFFERENCES IN PSYCHOLOGICAL AND BIOLOGIC VARIABLES BY TYPE OF COPING STRATEGY

VARIABLE	$\bar{X}$	SEM	p
<b>Anxiety</b>	8.41	0.564	< 0.01
Passive	10.63	0.714	–
Active	7.2	0.705	–
<b>Depression</b>	4.31	0.463	< 0.05
Passive	5.63	0.714	–
Active	3.6	0.571	–
<b>Psychological distress</b>	12.72	0.911	< 0.01
Passive	16.26	1.23	–
Active	10.8	1.12	–
<b>Cortisol (pg/ml)</b>	0.3	0.134	< 0.05
Passive	0.36	0.219	–
Active	0.26	0.162	–
<b>Tumor necrosis factor alpha (pg/ml)</b>	2.53	0.137	< 0.05
Passive	2.76	0.232	–
Active	2.41	0.161	–

SEM—standard error of measurement

**Note.** Coping was assessed with the Stress Coping Questionnaire, with scores ranging from 0 to 24, and with higher scores indicating a greater use of the coping style.

**“Passive coping rather than active coping has been associated with poorer immune response.”**

authors studied the effect of the pharmacologic treatment, the years since the end of treatment, and other sociodemographic variables, and did not find any significant differences.

## Results

Demographic characteristics and descriptive statistics for psychological and biologic variables are presented in Table 1. With the aim of being able to classify the participants based on the coping strategies in two groups, a cluster analysis using subscales of the SCQ was carried out on all breast cancer survivors. This analysis resulted in two final clusters, and the multivariate discriminant analysis was done to confirm the statistical validity of the established groups. The first cluster, designated as the active group ( $n = 35$ ), was characterized by a high level of focusing on a problem's solution. The second cluster, designated as the passive group ( $n = 19$ ), was characterized by women who exhibited negative self-targeting and avoidance behaviors. The passive group had more avoidance ( $F[1,52] = 10.385$ ;  $p < 0.01$ ) and negative self-targeting ( $F[1,52] = 39.172$ ;  $p < 0.001$ ) and less positive reappraisal ( $F[1,52] = 4.024$ ;  $p < 0.05$ ) and focusing on a problem's solution ( $F[1,52] = 18.419$ ;  $p < 0.001$ ) (see Table 2).

When analyzing the psychological data depending on the coping strategy to study the differences between these two groups, a significant effect was observed on anxiety symptom levels ( $F[1, 50] = 9.794$ ;  $p < 0.01$ ), depressive symptom levels ( $F[1, 50] = 6.056$ ;  $p < 0.05$ ), and distress levels ( $F[1, 50] = 9.592$ ;  $p < 0.01$ ). Specifically, women with passive coping strategy presented higher levels of these variables (see Table 3).

In the case of physiologic variables, the data revealed that there was a significant effect on cortisol ( $F[1, 50] = 4.538$ ;  $p < 0.05$ ) and TNF- $\alpha$  levels ( $F[1, 50] = 4.061$ ;  $p < 0.05$ ). Therefore, women with a passive coping strategy showed higher TNF- $\alpha$  and cortisol levels than women with an active coping strategy.

Table 4 lists the observed Pearson correlations between critical variables. The correlation analysis revealed a negative relationship between TNF- $\alpha$  and focusing on a problem's solution and positive reappraisal. Similarly, psychological distress correlated negatively with positive reappraisal and positively with negative self-targeting.

Negative self-targeting correlated negatively with focusing on a problem's solution and positive reappraisal. Finally, focusing on a problem's solution correlated positively with positive reappraisal.

Regression analyses were conducted to assess the predictive role of coping and biologic variables on psychological distress. First, psychological distress was introduced as the dependent variable. Predictors were the SCQ subscales, cortisol, and TNF- $\alpha$  levels. Next, with the aim to obtain the most parsimonious option that could explain the highest percentage of variance (Cohen, Cohen, West, & Aiken, 2003), nonsignificant variables were removed (such as biologic and psychological interactions). The general regression model obtained for psychological distress was significant ( $R^2 = 0.575$ ;  $F = 3.732$ ;  $p = 0.002$ ) (see Table 5).

## Discussion

The findings of this study report that a sample of breast cancer survivors with passive coping strategies had higher TNF- $\alpha$  and cortisol levels. In addition, based on coping strategies of these survivors, which focused on problem solutions and involved positive reappraisal, survivors' TNF- $\alpha$  levels were inversely correlated. The authors' results showed two different types of coping strategies in the examined sample of 54 breast cancer survivors. The passive group presented with higher scores on negative self-targeting and avoidance, and with lower scores on focusing on a problem's solution and positive reappraisal. The results also show differences in psychological distress depending on the coping strategy, finding higher anxiety and depression levels in women with passive coping. In addition, the authors found that lower scores on the avoidance and negative self-targeting and higher scores on positive reappraisal—both of which are characteristics of active coping—as well as higher scores for seeking social support, were associated with lower levels of psychological distress. In patients with breast cancer, emotion regulation strategies that have been found to be effective in decreasing psychological

**TABLE 5.** REGRESSION ANALYSIS FOR PSYCHOLOGICAL DISTRESS TO ANALYZE THE PREDICTIVE ROLE OF COPING, CORTISOL, AND CYTOKINE LEVELS

ITEM	$\beta$	t	p
Negative self-targeting	0.292	2.202	0.032
Open emotional expression	-0.103	-0.817	0.418
Avoidance	0.258	2.044	0.046
Seeking social support	-0.276	-2.366	0.022
Positive reappraisal	-0.288	-2.103	0.04
Cortisol	0.051	0.444	0.659
Tumor necrosis factor alpha	0.115	0.89	0.378

Note. Predictors were based on subscales of the Stress Coping Questionnaire.

distress include a positive reappraisal (Kvillemo & Bränström, 2014), whereas the avoidance coping strategy is associated with poor mood or depression (Bigatti, Steiner, & Miller, 2012; Malik & Kiran, 2013).

Few studies have shown the relationship between coping and these biologic variables. The results of a study by Sladek, Doane, Luecken, and Eisenberg (2016) found that perceiving greater stress than usual was associated with elevations in cortisol, but only for adolescents who were below average on engagement coping or coping efficacy. Regarding breast cancer survivors, positive coping behaviors are related to normal cortisol responses (Sjögren, Leanderson, & Kristenson, 2006). On the other hand, limited emotion regulation may exacerbate inflammation (Graham et al., 2006), whereas adaptive emotion regulation was associated with lower levels of inflammation (Appleton et al.,

**TABLE 4.** PEARSON CORRELATIONS BETWEEN SUBSCALES OF THE STRESS COPING QUESTIONNAIRE, PSYCHOLOGICAL DISTRESS, AND BIOLOGIC VARIABLES STUDIED

ITEM	TNF- $\alpha$	FOCUSED ON PROBLEM'S SOLUTION	NEGATIVE SELF-TARGETING	POSITIVE REAPPRAISAL	PSYCHOLOGICAL DISTRESS
Cortisol	0.158	0.095	0.176	-0.102	-0.022
TNF- $\alpha$	-	-0.352**	0.145	-0.35**	0.094
Focalized on problem's solution	-	-	-0.332*	0.339*	-0.184
Negative self-targeting	-	-	-	-0.374**	0.404**
Positive reappraisal	-	-	-	-	-0.312*

\*  $p < 0.05$ ; \*\*  $p < 0.01$   
TNF- $\alpha$ —tumor necrosis factor alpha

2013). In patients with breast cancer, strategies such as emotional acceptance moderate the associations between cytokines, such as TNF- $\alpha$ , and sickness symptoms (Reed et al., 2016). In addition, elevated levels of proinflammatory cytokines, including TNF- $\alpha$  and cortisol, are associated with numerous adverse health outcomes, such as coronary artery disease, osteoporosis, arthritis, and certain cancers (Currier & Nemeroff, 2014). Epidemiologic studies indicate that chronic inflammation predisposes individuals to various types of cancer, including breast cancer, and underlying inflammatory responses are linked to 15%–20% of all deaths from cancer worldwide (Munn, 2017). Chronic inflammation and chronic HPA axis dysregulation have been associated with tumor cell proliferation, angiogenesis, and mortality (Currier & Nemeroff, 2014; Villaseñor et al., 2015).

### Limitations

The limitations of this study include the convenience and size of the sample, which reduces intercultural reproducibility, and the lack of a control group. Additional cortisol samples may have provided a more accurate picture of HPA axis function. However, it was difficult to frequently collect plasma samples from breast cancer survivors because of poor adherence. Despite the limitations, this study points to one important recommendation for future research: Future studies with larger samples across socioeconomic and racial lines should attempt to consider the physiologic responses associated with specific coping strategies. In addition, it is recommended that a randomized controlled trial design be used to examine the impact of interventions targeting adaptive coping on psychological distress in breast cancer survivors. As such, therapies aimed at augmenting patients' repertoires of adaptive coping skills may not only help directly with psychosocial adjustment, but could also affect the HPA axis and the immune system, improving long-term health outcomes. Such interventions would be a highly effective and feasible next step in improving survivors' quality of life.

### Implications for Nursing

Great advances have been made in the diagnostic and treatment aspects of cancer care, and the need for specific survivorship care delivery models has been stressed (Hebdon, Abrahamson, Griggs, & McComb, 2018; Sabiston, Lacombe, Faulkner, Jones, & Trinh, 2018). Although more research is required, passive coping style may be a modifiable risk factor associated with inflammation, disrupted HPA axis, and psychological distress in this population. Therefore, the identification of survivors' maladaptive coping strategies by nurses and the subsequent personalized goal-directed support may meet the needs of these women, preventing, in turn, the hazardous stress-derived elevations of TNF- $\alpha$  and cortisol. Of note, coaching on active coping strategies seems to be closely related to the promising self-advocacy training for cancer survivors, because this last concept is defined

### IMPLICATIONS FOR PRACTICE

- Understand that high scores of negative self-targeting and avoidance, and high levels of cortisol and tumor necrosis factor alpha, can elicit psychological distress.
- Educate nurses that coping skills modulate distress, and distress can lead to hazardous physical and psychological states.
- Assess breast cancer survivors for psychosocial and emotional needs and identify active and passive coping strategies.

as an individual's ability to get his or her needs and priorities met in the face of a challenge (Hagan & Donovan, 2013; Hagan et al., 2018). However, given the pronounced individuality of the survivorship experience (Hebdon et al., 2018), a better understanding of psychobiologic factors in the emotional state of breast cancer survivors is critical to develop an integrative praxis on distress prevention and caregiving.

### Conclusion

The results of this study show that the coping strategy is an important variable in determining psychological distress for breast cancer survivors. In addition, immune and endocrine differences were found depending on coping strategy used. Specifically, breast cancer survivors with passive coping had higher psychological distress and higher levels of TNF- $\alpha$  and cortisol, which might indicate a higher vulnerability to developing certain pathologies. To provide integrative oncologic care, it is necessary to understand the contribution of the coping styles and different physiologic variables in the emotional state, which could help when applying an individualized biopsychosocial approach for cancer survivors. The data potentially enable applications to be developed, such as psychological interventions for patients or survivors with passive coping strategies, aimed to modulate the risk of psychological distress or adopt a better interprofessional intervention for breast cancer survivors.

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