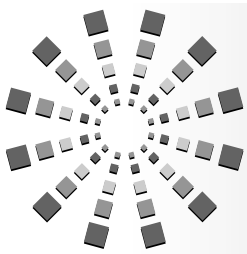

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Quality of Life in Women With Breast Cancer Receiving Chemotherapy and the Moderating Role of Cortisol

KEYWORDS
Breast neoplasms
Chemotherapy
Hydrocortisone
Quality of life

Background: Quality of life (QoL) is severely affected by breast cancer (BC) and its treatment, particularly chemotherapy treatment. Psychological morbidity, illness perceptions, and self-efficacy for coping are important variables that impact QoL during the treatment of BC. The impact of cortisol on QoL has been poorly studied. **Objective:** The aim of this study was to identify the contributing variables to QoL in women with BC receiving adjuvant chemotherapy, as well as the moderating role of cortisol in the relationship between treatment adverse effects and QoL. **Methods:** This cross-sectional study included 112 women with BC undergoing chemotherapy who answered the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire, the Supplementary Questionnaire Breast Cancer Module, the Illness Perception Questionnaire, the Cancer Behavior Inventory—Brief Version, and the Hospital Anxiety and Depression Scale. In addition, salivary cortisol concentrations were also assessed. **Results:** The strongest contributor to lower QoL was treatment adverse effects. The illness perception and the cancer stage also contributed to a lower QoL. Nadir cortisol moderated the relationship between adverse effects and QoL. **Conclusion:** Breast cancer chemotherapy and illness perceptions, even at the beginning of treatment, showed a great impact on QoL. **Implications for Practice:** It is important during chemotherapy to assess women's illness perceptions, as well as their stress levels to help women cope with the stress associated with treatment adverse effects. Monitoring cortisol is important as cortisol moderated the relationship between adverse effects and QoL. For those women struggling with stress, a reference to a mental health provider is warranted.

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According to the World Health Organization,[1] breast cancer (BC) is the most common cancer among women, affecting 2.1 million women each year globally and causing the greatest number of cancer-related deaths among women. Ferlay et al[2] estimated that in 2018, 626 700 women died of BC.

Cancer is characterized by abnormal cells that grow and invade healthy cells in the body. More specifically, in BC, abnormal cells appear in the breast, and depending on their proliferation factor, they may invade the surrounding tissues (eg, axilla) or spread (metastases) to other areas of the body.[3] Type of BC, stage of cancer, patient's general condition, age, and tumor localization[4] are important factors to consider in treatment options.

Patients in more advanced cancer stages and undergoing adjuvant endocrine therapy and chemotherapy report more symptoms, less functionality and lower quality of life (QoL). Sociodemographic variables, such as being younger, unemployed, less educated and having lower income, have a negative impact on QoL,[5–7] as well as clinical variables, namely, cancer stage,[5,7] different treatments,[8] number of treatment cycles,[9] adverse effects of chemotherapy treatment,[10] symptoms,[11] and functional status.[12] Quality of life has been reported as being at its lowest during the third cycle (in 6) and highest in the first cycle.[9] Adverse effects of the systemic treatment, such as nausea and vomiting, insomnia, fatigue, and hair loss, are associated with worse QoL.[5]

In women with BC, QoL is also affected by illness perceptions,[13] self-efficacy for coping with cancer,[14] depression, anxiety,[15,16] and distress.[17] Cortisol is involved in the regulation of bodily processes, such as mood, energy, immune system management, and in the control of stress reactions.[18] Cortisol has also been associated with QoL in patients with BC.[19]

Elevated evening cortisol concentrations were associated with poorer psychosocial and physiological outcomes in BC patients.[19] The levels of cortisol throughout the day may be dysregulated when there is exposure to stress. Dysregulated levels in the morning, such as cortisol awakening response (CAR), have been associated with negative physical and health outcomes with negative repercussions on QoL.[20,21] However, most of the studies in this field have been carried out on women with severe and metastatic BC, with endometriosis or with chronic pelvic pain,[22–25] and there are few studies in women with early-stage BC. In a study that included women with BC stage I, II, or III, the participants' diurnal cortisol rhythm was found to be normal.[26] Therefore, because of the scarcity and design inconsistency of studies addressing the relationships among physiological variables (eg, cortisol), psychological variables, and QoL in the early stages of BC, this study aims to help fill this knowledge gap.[27] Moreover, the inclusion of a psychophysiological stress indicator, such as cortisol, is important because when dysregulated it tends to be associated with negative physical and psychological consequences and an impact on health outcomes, such as cancer progression.[24,28]

■ Study Conceptual Framework

To understand the relationships between sociodemographic, clinical, psychophysiological variables and QoL in BC, this study was based on Livneh's[29] Model of Psychosocial Adaptation to Chronic Disease. Because the process of adaptation to chronic disease is dynamic, Livneh's[29] model comprises 3 phases, with the main outcome being QoL. The first phase is called *antecedents*, which include the events that are directly or indirectly related to the onset of the disabling condition. The second phase is the *adjustment process* (focus of the present study), which includes the initial reactions and responses to the disease and includes contextual variables, such as sociodemographic variables (eg, age, marital status, level of education), clinical variables (eg, phase and duration of cancer, number of chemotherapy cycles, type of surgery, adverse effects), and environmental characteristics, associated with psychological attributes and personality traits (eg, illness representations and self-efficacy for coping).

Quality of life is assessed in the physical and mental dimensions. The model also postulates moderation or mediation analyses between contextual influences and QoL. Based on the theoretical model and taking into consideration the transversal design that does not allow for temporality, the purpose of this study was to analyze the variables that contribute to QoL and to assess the moderating role of cortisol in the relationship between treatment adverse effects and QoL. We hypothesized that (1) stage, adverse effects, psychological morbidity, self-efficacy for coping, and illness perceptions will contribute to QoL, and (2) cortisol (CAR and nadir) will moderate the relationship between treatment adverse effects and QoL.

■ Methods

Participants

Data were collected in 4 hospitals in the North of Portugal. The sample comprised 112 participants diagnosed with early-stage BC, and the criteria for inclusion were as follows: (1) a diagnosis of BC at stage I or II; (2) being at least 18 years old; (3) receiving adjuvant chemotherapy treatment; (4) levels 0 to 2 on the Eastern Cooperative Oncology Group Performance Status[30]; and (5) health literacy, assessed through the Short Assessment of Health Literacy.[31,32] Scores less than 14 equated to inadequate literacy, and this became an exclusion criterion. The other exclusion criteria were as follows: a diagnosis of a psychiatric disorder (eg, psychosis) and cognitive deficit reported in the patient's medical chart.

Procedure

This descriptive and quantitative cross-sectional study was approved by the ethics committee of the 4 hospitals where the study was took place. This study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and in line with the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals.

One of the researchers attended breast group consultations postsurgery, getting acquainted with BC patients who met the inclusion criteria for the study. In the breast group consultation, the number of chemotherapy cycles that each participant would undergo was defined, as well as its regimen and respective dosages.

Subsequently, an oncology appointment was scheduled prior to the chemotherapy treatment to inform the patient about the treatment, addressing the possible symptoms that could arise. After this consultation, and if no exclusion criteria (eg, lack of autonomy, difficulties with listening and writing comprehension, and severe psychiatric disorder) were present, women were invited by one of the researchers to participate in the study, and once accepted, they signed the informed consent form.

For the collection of saliva to assess salivary cortisol, Salivette® (Sarstedt, Germany) was used. After the medical consultation, women who met the inclusion criteria and who agreed to participate were provided with an envelope containing 6 Salivette®: 3 to be collected the next day to obtain baseline measurements and another 3 Salivette® to be collected the day before chemotherapy treatment. A leaflet explaining the saliva collection procedure and its storage was made available. On the day before the second cycle of chemotherapy (when participants were assessed), the participants had their saliva collected around 11 PM (the lowest peak of the cortisol pattern) and were advised to be 30 minutes before this collection without eating, drinking, smoking, or taking medications.

On the day of chemotherapy, shortly after waking up and 30 minutes later (CAR assessment), while fasting, they completed another saliva collection. Thus, 3 saliva samples were collected to assess the cortisol nadir and the CAR, which reflect cortisol levels based on the difference between 30 minutes and awakening.[33]

Saliva samples were collected prior to chemotherapy treatment (6 Salivette®), and at the time of the assessment protocol, which included the sociodemographic and psychological measures. Clinical information was collected from physicians at the time of the breast group consultation.

Instruments

SOCIODEMOGRAPHIC AND CLINICAL QUESTIONNAIRE

This questionnaire includes questions regarding sociodemographic variables (eg, age, marital status, educational level, current professional status, and duration of the disease) and clinical data (eg, cancer stage; number of cycles schedule; type of surgery, sentinel lymph node, and presence of physical comorbidities).

RESEARCH AND TREATMENT OF CANCER QUALITY OF LIFE QUESTIONNAIRE

The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire assesses QoL in cancer patients and includes 30 items, divided into 9 scales: 5 functional subscales (physical, cognitive, emotional, role, and social), 3 symptom scales (fatigue, pain, and nausea/vomiting), and a global health and QoL scale.[34,35] The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire has unique items related to loss of appetite, insomnia, dyspnea, constipation, diarrhea, and financial difficulties. Higher scores indicate better QoL. In the original version, Cronbach's alpha (α) for the several subscales ranged from .52 to .89 and in the Portuguese version from .57 to .88. In this study, only the full scale was used, with an α of .86.

SUPPLEMENTARY QUESTIONNAIRE BREAST CANCER MODULE

This instrument consists of 23 items evaluating the effects of adjuvant treatments on women in treatment for BC.[36,37] The questionnaire includes 4 scales of symptoms (breast and arm symptoms, upset by hair loss, and systemic therapy side effects) and function (body image, future perspective, sexual functioning, and sexual enjoyment). Higher scores indicate worse QoL regarding the symptom scale and better QoL in the function scales. Cronbach's alpha (α) in the original version ranged from .46 to .94 for the subscales. In this study α ranged between .65 and .87; only the subscale systemic therapy side effects was assessed, with an α of .60.

ILLNESS PERCEPTION QUESTIONNAIRE—BRIEF

This questionnaire assesses perceptions of the disease on a Likert scale of 0 to 10.[38,39] It consists of 9 items, divided into 3 subscales: cognitive perceptions (consequences, duration, personal control, treatment control and identity), emotional perceptions (concerns and emotions), and understanding of the disease and causal representations (not used in the study). A high global score indicates more threatening perceptions.[38] In the original scale, the test-retest reliability was good (Pearson correlations 0.24–0.73). In this study, the α for the full scale was .75.

CANCER BEHAVIOR INVENTORY—BRIEF VERSION

This instrument assesses self-efficacy for coping in cancer patients.[40,41] It consists of 12 items on a Likert scale from 1 (not at all confident) to 9 (totally confident), where higher scores indicate greater self-efficacy in treating cancer-related tasks. In the original version, the Cronbach's alpha (α) was .84 and in the Portuguese validation was .88. In this study, the α was .92.

HOSPITAL ANXIETY AND DEPRESSION SCALE

This scale, with 14 items, assesses depression and anxiety in patients with physical conditions and in outpatient treatment.[42,43] The instrument includes 2 subscales: anxiety and depression, each with 7 items, on a 4-point Likert scale (0 = nonexistent, 3 = very severe). Higher scores indicate higher levels of anxiety or depression, according to the respective subscale or psychological morbidity (full scale). In the Portuguese version, the Cronbach's alpha (α) were .76 for anxiety and .81 for depression. In this study, the full scale was used with an α of .90.

Salivette® (Sarstedt, Germany) were used for the collection of saliva, and IBL International ELISA kits (Cortisol Saliva ELISA; IBL International, Germany) were used to assess salivary cortisol concentrations according to the protocol stipulated by the kits. In the present study, the nmol/L unit of measurement was applied using the conversion formula provided by IBL International: cortisol (μg/dL) × 27.6 = nmol/L. The intra-assay coefficient of variation was less than 5% (2.18%).

Statistical Analysis

Data were analyzed with IBM SPSS Statistics for Windows, version 25 (IBM Corp, Armonk, New York). Based on Daniel Soper's sample size calculator, taking into account the anticipated

effect size (f2) of 0.15, desired statistical power level of 0.80, 5 independent variables (correlated with QoL), and probability level of 0.05, a minimum of 91 participants was required. After evaluating the assumptions for the use of parametric tests, an independent-samples t test was performed to assess differences in cortisol samples according to presence/absence of physical comorbidities; Pearson correlation and point-biserial tests were also performed to evaluate the correlation between sociodemographic, clinical, and psychological variables with QoL. To determine the variables that contribute to QoL, a hierarchical multiple regression (stepwise method) was performed. The variables selected were those that correlated significantly with QoL (stage, adverse effects, psychological morbidity, illness perceptions, and self-efficacy for coping), after meeting the underlying assumptions. Finally, the PROCESS command for SPSS version 3.3 and the Johnson-Neyman (JN)[44] technique were used to evaluate the moderating role of nadir cortisol in the relationship between adverse effects and QoL. The moderating role of CAR was not evaluated because the assumptions for performing the statistical analysis were not met since CAR was not associated with QoL.

■ Results

Sample Characteristics

The sample consisted of 112 participants with BC, aged between 27 and 73 years (mean, 52.67 [SD, 10.29]). Approximately 3.0% of the sample was receiving the adriamycin-cyclophosphamide (AC) cytostatic regimen, with a 3-week interval between each cycle; approximately 21.4% were receiving 5-fluorouracil/epirubicin/cyclophosphamide followed by a docetaxel regimen, with a 3-week interval between each cycle; another 9.8% were receiving the regimen of AC followed by docetaxel, with a 3-week interval between each cycle; and 35.7% were receiving AC followed by paclitaxel, with a 3-week interval between the first 4 cycles (AC) and a 1-week interval between the remaining 12 cycles. In terms of the percentage of participants per hospital, 66.1% (n = 74) enrolled from hospital A, 21.4% (n = 24) from hospital B, 9.8% (n = 11) from hospital C, and 2.7% (n = 3) from hospital D. There were no statistically significant baseline differences between participants with physical comorbidities and those without comorbidities on nadir cortisol (t_{70} = 0.597, P = .552), cortisol upon waking (t_{70} = −0.789, P = .433), and cortisol 30 minutes after waking (t_{45} = 0.198, P = .844). Other sociodemographic and clinical information is shown in Table 1.

Variables That Contributed to QoL

Based on the correlational analyses, the results of the regression analysis showed that stage, treatment adverse effects, and illness perceptions contributed to QoL. The adverse effects explained 47.4% of the total variance of QoL, resulting in a statistically significant R^2 of 0.479, $F_{1,110}$ = 100.987, P < .001 (model 1). The addition of cancer stage to the prediction of QoL (model 2) explained 2.8% of the total variance, which is statistically significant, R^2 of 0.497, $F_{1,109}$ = 6.128, P < .05. Finally, the addition of illness perceptions explained 7.4% of the total variance of QoL, also statistically significant, R^2 of 0.569, $F_{1,108}$ = 19,123, P < .001. The final model explained 58.1% of the total variance R^2 = .581, $F_{3,108}$ = 49.846, P < .001, R^2 adjusted = 0.569. The model showed that more adverse effects (β = −.523, t = −7.383, P < .001), more advanced cancer stage (β = −.135, t = −2,128, P < .05), and more threatening illness perceptions (β = −.311, t = −4.373, P < .001) predicted lower QoL (Table 2). Therefore, the first hypothesis that cancer stage, adverse effects, psychological morbidity, self-efficacy for coping, and illness perceptions would contribute to QoL was partially confirmed.

CORTISOL NADIR AS A MODERATOR IN THE RELATIONSHIP BETWEEN TREATMENT ADVERSE EFFECTS AND QOL

The model that tested the moderating role of nadir cortisol in the relationship between adverse effects and QoL was significant, $F_{3,104}$ = 39,8115; P < .001; β = .0460; 95% confidence interval, 0.0071–0.0848; t = 2.3481; P = .0208, explaining 53.45% of the variance. The JN technique was used to determine the transition point where nadir cortisol was sufficient to detect a difference in the relationship between treatment adverse effects and QoL (at the .050 level).[44] The JN showed that treatment adverse effects were significantly correlated with QoL when the standard value of nadir cortisol was 6.57 below the mean (β = −.3315, P = .05), corresponding to 93.52% of the sample (Figure). Therefore, the second hypothesis that stated nadir cortisol would moderate the relationship between treatment adverse effects and QoL was confirmed.

■ Discussion

The aim of the study was to identify the contributing variables to QoL in women with early-stage BC receiving adjuvant chemotherapy, as well as the moderating role of cortisol in the relationship between treatment adverse effects and QoL. The results of the present study were similar to other studies regarding the negative impact of treatment adverse effects,[45] threatening perceptions,[46] and psychological morbidity on QoL.[47] However, QoL in this study was higher compared with previous studies.[13,48] Also, cancer stage, treatment adverse effects, and illness perceptions contributed to QoL; that is, more adverse effects contributed negatively to QoL. In fact, BC treatment interferes with women's well-being and daily activities[8] and is associated with anxiety, fear of death, and worse QoL.[9] Cancer stage also contributed negatively to QoL as expected because QoL becomes worse as the disease stage increases,[49] although in Gangane and colleagues,[6] study with 208 women in stages 1 to 4, this association was not found. Nonetheless, women in the early stages of BC report fewer symptoms than women in more advanced stages, as well as less anxiety and depression,[15] with a lower impact on QoL.[13] Certainly, women with early stage of BC undergoing chemotherapy may experience more burden symptoms and a poorer QoL than early-stage women who do not receive chemotherapy.[49]

Illness perceptions also contributed negatively to QoL, ie, more threatening illness perceptions contributed to worse QoL. The literature also showed a negative association between

Table 1 • Clinical and Sociodemographic Characteristics of the Sample (N = 112)

	n (%)	Mean (SD)	Min	Max
Quality of life (EORTC QLQ-C30)	112	72.93 (15.47)	32	98
QLQ-BR23 (treatment adverse effects)	112	31.42 (15.01)	5	57
Illness perceptions (IPQ-B)	112	35.72 (11.86)	0	62
Self-efficacy for coping (CBI)	112	78.48 (12.39)	39	99
Psychological morbidity (HADS)	112	10.37 (6.82)	0	30
Age, y	112	52.67 (10.29)	27	73
Duration of cancer, mo	112	3.96 (1.51)	1.50	7
Marital status				
Unmarried[a]	25 (22.3)			
Married/common law marriage	87 (77.7)			
Education levels				
Basic education (9 y)	73 (65.2)			
Secondary education (3 y)	22 (19.6)			
University	17 (15.2)			
Professional status				
Active worker	4 (3.7)			
Sick leave	69 (61.6)			
Others conditions[b]	39 (34.7)			
Stage (TNM)[c]				
T1	43 (38.4)			
T2	69 (61.6)			
No. of cycles schedule				
4	37 (33)			
6	24 (21.4)			
8	11 (9.8)			
16	40 (35.7)			
Type of surgery				
Breast-conserving surgery	90 (80.4)			
Mastectomy	7 (6.3)			
Bilateral mastectomy	2 (1.8)			
Modified radical mastectomy	13 (11.6)			
Sentinel lymph node				
Positive	52 (46.4)			
Negative	60 (53.6)			
Physical comorbidity				
No	78 (70.4)			
Yes	34 (29.6)			
Hypertension	16 (14.3)			
Rheumatoid arthritis	1 (0.9)			
Diabetes	5 (3.6)			
Hypertension and dyslipidemia	4 (3.6)			
Glaucoma	1 (0.9)			
Diabetes and dyslipidemia	1 (0.9)			
Dyslipidemia	3 (2.7)			
Hypertension and diabetes	3 (2.7)			

Abbreviations: CBI, Cancer Behavior Inventory; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire; HADS, Hospital Anxiety and Depression Scale; IPQ-B, Illness Perception Questionnaire—Brief; M, median; Max, maximum; Min, minimum; n, frequency distribution; QLQ-BR23, European Organization for Research and Treatment of Cancer Breast Cancer–Specific Quality-of-Life Questionnaire; TNM, tumor size, lymph node status, distant metastasis.

[a]Included single, divorced, and widow.

[b]Included unemployed; reformed and domestic.

[c]The TNM classification for staging of breast cancer.

perceptions about BC and QoL.[13] Figueiras and colleagues[39] assert that cancer perceptions are related to clinical and behavioral factors, as these can exacerbate the negative symptoms of the disease (eg, pain) or improve the prognosis (eg, adherence to treatment). Illness perceptions directly influence emotional response to the disease[50] and coping behavior, impacting QoL.[51] When illness perceptions are more threatening, patients have a deeper perception of the symptoms, perceiving the disease as lasting longer and report having less control over their recovery.[50] The lack of information regarding the etiology and prognosis is associated

Table 2 • Variables That Contribute to QoL Using the Stepwise Method

	QoL					
	Model 1		Model 2		Model 3	
Variable	β	t	β	t	β	t
Treatment adverse effects	−0.692	−10.049[c]	−0.663	−9.719[c]	−0.23	−7.383[c]
Cancer stage			−0.169	−2.476[a]	−0.135	−2.128[a]
Illness perceptions					−0.311	−4.373[c]
R^2		0.479		0.497		0.569
F		100.987[c]		55.912[c]		49.846[c]
$\triangle R^2$		0.479		0.028		0.074
$\triangle F$		100.987		6.128		19.123

Abbreviations: β, standardized β values; F, F test; $\triangle F$, F test change; QoL, quality of life; $\triangle R^2$, R^2 change.
[a]$P < .05$.
[b]$P < .01$.
[c]$P < .001$.

with greater fear and uncertainty, which is associated with lower overall well-being.[52]

In this study, contrary to what was predicted based on other studies,[16,53] there was no contribution of psychological morbidity (anxiety and depression) to QoL. There is evidence that, in the first cycle of chemotherapy treatment, the most prevalent psychological symptoms are anxiety, increasing until the third cycle of treatment.[54,55] Depression, despite being a prevalent symptom, is more pronounced during the course of treatment.[9] One may hypothesize that in this particular sample, probably due to the fact that the majority (80.04%) had undergone conservative surgery, treatment adverse effects in the early stage of the disease may be the focus of women's concerns. This hypothesis should be tested in a longitudinal design to analyze whether physical symptoms are of a greater concern than emotional reactions, over time, and their impact on QoL.

Regarding self-efficacy for coping, it is important to describe the primary and secondary appraisal[56]: primary appraisal is an assessment of how significant an event is, including whether it is a threat or an opportunity (cognitive appraisal); secondary appraisal considers one's ability to cope or take advantage of the situation. In the first cycle of treatment, women may be more focused on the physical symptoms caused by treatment, and therefore cognitive appraisal, namely, illness perceptions, may become paramount. This result was found in this study emphasizing the primary appraisal of the stressful event (eg, chemotherapy).[57] Later on, women may be more concerned with coping options (secondary appraisal) to effectively handle the sources of stress. For this reason, self-efficacy for coping may not yet be so evident, because women are probably still processing adverse effects from a primary appraisal perspective. Future studies should test this hypothesis, because the evidence is controversial in terms of the trajectory of self-efficacy over time, in the cancer population.[58,59]

The results revealed that nadir cortisol levels had a moderating role in the relationship between adverse effects and QoL. Thus, adverse effects were negatively correlated with QoL when nadir

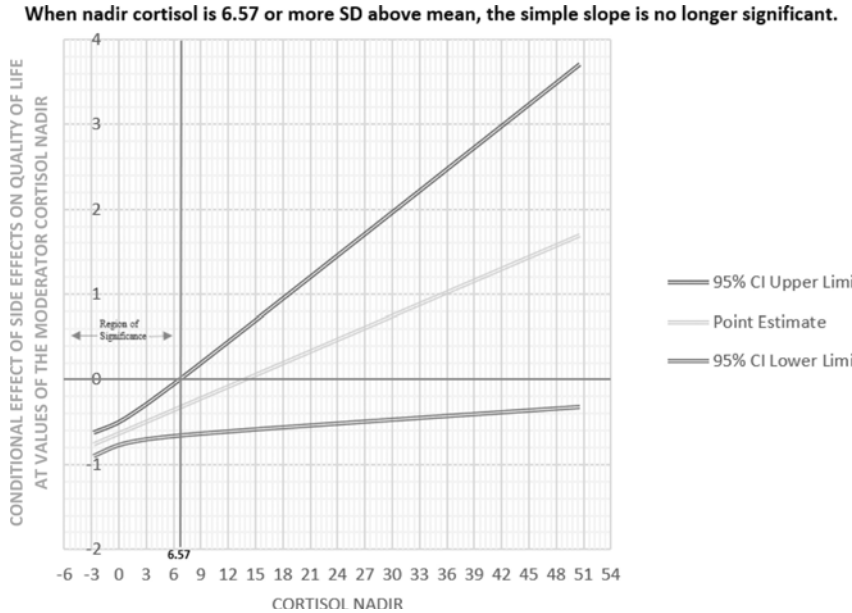

Figure ■ Moderating role of the cortisol nadir in the relationship between adverse effects and quality of life.

cortisol levels were low.[19] Treatment-related symptoms are major stressors for BC patients with an impact on QoL.[10] It is known that the adverse effects can cause, per se, physiological alterations,[60] which are aggravated by women's anxiety in the first treatments,[9] and when cortisol levels are high, there is a suppression of the immune system.[24] Therefore, low levels of nadir cortisol (considered normal)[61] reveal a better immune system response that reduces the treatment adverse effects[18] and, as a consequence, contributes to a better QoL.[10] It is expected that these normative values in cortisol may be more common at an early stage of treatment. However, with continued exposure to the stressor stimulus (chemotherapy and its adverse effects), as well as increased toxicity of cytostatic agents and their cumulative effect,[62] the values may assume a more altered pattern, because of hypothalamic-pituitary-adrenal axis dysregulation, with health consequences.[63] In fact, many of the studies revealed changes in cortisol values, but the assessment was done in advanced stages of treatment.[23–25] Thus, in future studies to promote QoL, it would be important to study salivary cortisol under the same conditions and in a comparative perspective: in the initial and final phases of treatment.

This study highlighted the applicability of Livneh's[29] model to cancer disease in a cross-sectional design. Because adjustment to chemotherapy treatment, is the complex and interactive process involving a panoply of variables, based on this model, the results showed that salivary cortisol may be an important moderating variable in the relationship between contextual factors (adverse effects) and QoL. Likewise, one may understand, at this cancer stage, which variables contribute to a better QoL, considering the interconnectedness of the constructs the model comprises. Finally, the model may also help to design future longitudinal research studies considering the stages of adaptation to cancer.

Limitations

There are some limitations that must be considered in the present study. The transversal design that does not allow cause-effect relationships is a limitation as is that instruments were mostly self-reported. Finally, the fact that most women in the sample had conservative breast surgery requires caution in the generalization of the results.

Future Implications

Future studies should replicate this study in a longitudinal design controlling for cancer stage, type of surgery, and the moderating role of CAR over time, following the theoretical model that allows the study of the illness trajectory over time in 3 phases. In fact, Livneh's[29] model as a theoretical framework was adequate for the purpose of the study. According to results, to promote QoL in clinical practice, it would be important to assess cortisol levels (eg, Phillips and colleagues'[64] study), particularly in women with high stress/anxiety, in the beginning of treatment. It would also be important to study the trajectory of self-efficacy in women undergoing chemotherapy treatment to help the adjustment to BC,[59] and promote their QoL.

■ Conclusion

Women with BC, at the beginning of the second cycle of chemotherapy, who report more treatment adverse effects, who are at a more advanced stage, and who have threatening illness perceptions reported lower QoL. Thus, chemotherapy—even in the beginning of treatment—had a negative impact on QoL. As a result, it is crucial that intervention programs focus on adverse effects, cancer stage, and illness perceptions in order to minimize their impact on women's QoL over time. In view of the evidence in the literature and the present results, the relationship between adverse effects and QoL in women with early-stage BC needs to be highlighted, with adverse effects being the main contributors to QoL.

Nadir cortisol played a moderating role in the relationship between adverse effects and QoL. Cortisol (a physiological correlate of stress/anxiety) has been poorly studied in patients, undergoing adjuvant treatment, in the early-stages BC, despite being extensively studied in survivors and those at advanced stages. However, cortisol levels may play an important buffer role early on, when women are still undergoing chemotherapy treatment. Thus, the results of this study emphasize the importance of assessing women's stress/anxiety levels, as a possible carrier of physiological changes, in the beginning of treatment, in order to effectively intervene on chemotherapy adverse effects and, as a result, on women's QoL.

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