Original article

Effects of pessimism, depression, fatigue, and pain on functional health-related quality of life in patients with resected non-advanced breast cancer

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ABSTRACT

Introduction: The aim was to analyze the effects of pessimism, depression, fatigue, and pain on functional health-related quality of life (HRQoL) in patients with resected, non-advanced breast cancer.
Methods: A prospective, multicenter study was conducted in 440 breast cancer patients. They completed the Brief Symptom Inventory (BSI), the European Organization for Research and Treatment of Cancer QoL-Questionnaire-Core-30 (EORTC-QLQ-C30), and the Revised Life Orientation Test (LOT-R).
Results: Prevalence rates of pessimism and depression were 23.3% and 40.0%, respectively. Fatigue and pain were the most common symptoms, 8.8% and 4.2%, respectively. Patients without a partner were more pessimistic that partnered ones; those with a lower level of education and subjects without a partner exhibited more depression. Depression was a major factor that proved to have the greatest explanatory power for HRQoL (physical, role, emotional, cognitive, and social functioning) and global health status (R^2 range: 0.13 to 0.39). Of the five domains, fatigue had a significant effect on four and pain, on two.
Conclusion: This study reveals the impact of depression and pessimism on physical, psychological, social, and quality-of-life aspects and the importance of evaluating them in patients who are going to initiate adjuvant chemotherapy for breast cancer.

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1. Introduction

Breast cancer is the most common of all cancers among women around the world, affecting one in every twelve, accounting for 25% of all cancers in females [1], and causing 571,000 cancer deaths every year [2]. It is diagnosed when its sufferers are still relatively young, around 55 years of age [3]. Surgery is the treatment of choice for non-metastatic cancer; chemotherapy and radiotherapy are adjuvants that lower the risk of recurrence at all stages of the disease [3].

The most frequent physical and psychological symptoms in patients during and after overcoming breast cancer include fatigue, perceived pain, and depression [4–7]. Fatigue, experienced by three quarters of the women with breast cancer, is the single most common physical symptom [4,8,9] and can last for months, even ten years post-treatment [10]. Depression, experienced by between 18% and 54.4%, is one of the most prevalent psychological symptoms in patients both during treatment and once breast cancer has been overcome [5,6,11,12]. Pessimism is an important psychological construct that can predict the individual's reaction to stress and has been defined as the degree to which a person expects negative

experiences in the future [13]. Pessimism helps to explain the variability in the amount of psychological distress in patients with breast cancer [14]. In general, patients who were pessimistic scored significantly lower on quality of life (QoL) *versus* those who were not [15].

Patients with breast cancer are three time more likely to experience physical symptoms and psychological distress than patients with other types of tumors due, largely, to treatment side effects and secuelae [12,16]. Physical and psychological symptoms decrease these women's psychological wellbeing and their quality of life after diagnosis, when initiating treatment, and after being cured [4,17]. However, in most oncological settings, treatment focuses mainly on the physical symptoms, while psychological distress often goes unnoticed. Analyzing the effect of physical and psychological symptoms in patients with breast cancer is pertinent because it can aid in planning treatment and increasing therapeutical success, enhancing patients' quality of life, their recovery, and return to their occupational, family, and social activities.

The purpose of this prospective study was to evaluate pessimism, depression, fatigue, and pain, as well as their effects on the functional status and quality of life of patients with breast cancer after surgery and prior to beginning adjuvant treatment.

2. Material and methods

2.1. Methods

This prospective, multicenter, cross-sectional study was conducted in 15 Spanish hospitals by researchers from the Continuous Care Group of the Spanish Society of Medical Oncology (SEOM). The study was approved by the institutional research ethics committee of each hospital, by the Spanish Agency for Medicines and Health Products (AEMPS) and informed written consent was obtained from participating patients. Patients undergoing surgery for non-metastatic breast cancer and candidates for adjuvant chemotherapy were included consecutively between September 2015 and August 2018. Patients who would only receive adjuvant hormonotherapy and/or radiotherapy were excluded.

2.2. Measures

The socio-demographic characteristics and clinical variables of the participants were obtained from the institutions where they received treatment. Depression, pessimism, quality of life, and the physical symptoms of fatigue and pain were measured using questionnaires that each patient completed after the first visit with the medical oncologist during which they were informed of the need to receive adjuvant chemotherapy and prior to starting said treatment. The reason for doing this at this time was to understand their physical and psychological status, as well as their personal resources before actually beginning cancer treatment with adjuvant chemotherapy. Thus, patients had several days to fill in the questionnaires at home and could clarify any doubts with their medical oncologist before submitted the completed forms.

Depression was evaluated using the Brief Symptom Inventory (BSI) [18]. The BSI included 6 items asking about patients' perception of feeling tense, worried, depressed, and irritable by assessing the affective aspects of depression and general distress [18]. Items used a five-point Likert scale (0—4) and a one-week recall period. Raw scores were converted to T-scores based on gender-specific normative data from non-patient normal, with higher scores indicating higher depression levels. The cut-off point for depression was as per this instrument (cutoff T ≥ 63) [18]. In the present study, Cronbach's α was 0.74.

Pessimism was assessed with the Revised Life Orientation Test

(LOT-R) [13], a 6-item measure of individual differences in dispositional optimism and pessimism. Items are rated from 1 (strongly disagree) to 5 (strongly agree). Raw scores are transformed on a 0—100 scale; scores of <50 indicate a tendency to expect more negative outcomes. In our sample, Cronbach's α for the scale was 0.87.

QoL was appraised using the European Organization for Research and Treatment of Cancer QoL (EORTC QLQ-C30) [19], which was specifically designed for cancer patients. It includes five functional scales (physical, role, cognitive, emotional, and social), a global health status/QoL scale. Scores for each item range from 0 to 100. Higher functional and global health status scores indicate better QoL. Scores of <75 indicate a clinically relevant symptom, while scores ≥75 indicate that the symptom in question does not represent a problem [20]. In our sample, Cronbach's α value for this scale was 0.89.

Fatigue and pain were rated on the symptom subscale of the **EORTC-QLQ-C30** [18]. These subscales consist of six items inquiring about patients' perception of feeling weak, pain, and needing to rest. Items are scored on a four-point Linkert scale from 0 ("not at all") to 4 ("very much") and a one-week recall period. Raw scores are transformed on a 0—100 scale with higher scores representing worse quality of life. Scores of ≥75 indicate a clinically important symptom and scores <75 suggest that the symptom is not a problem [20].

2.3. Statistical analysis

Descriptive statistics were used to analyze participants' socio-demographic and clinical characteristics. Chi-square tests were conducted to compare differences in participants' socio-demographic and clinic characteristics with or without physical and psychological problems. Multiple logistic regression analyses were performed to examine the effects of pessimism, depression, fatigue, and pain on the HRQoL functional scale, with adjustment for sociodemographic and clinical variables. Those sociodemographic and clinical variables that were significantly related to physical and psychological problems in the univariate analysis were introduced into the logistic regression analysis as adjustment variables using the forward conditional method for logistic regression. We applied Nagelkerke's R-squared to determine goodness-of-fit of the logistic regression model [21]. For all analyses, a significance level of α < 0.05 was used. Analyses were run on the IBM-SPSS 23.0 statistical software package for Windows PC.

3. Results

3.1. Patient baseline characteristics

Subjects' mean age was 53.2 years at study entry. The patients in this sample were mostly married or in a relationship (71.7%); 22.1% had a university education, and 55.8% were active. Most had stage I—II breast cancers (89.1%) and were going to receive adjuvant chemotherapy and radiotherapy (66.3%); see Table 1.

3.2. Prevalence of pessimism, depression, fatigue, and pain

The prevalence of pessimism (LOT score <50) was 23.3% and 40% for depression (BSI T score ≥ 63). The prevalence of fatigue and pain (Raw score ≥ 75) were 8.8% and 4.2%, respectively. The results of the univariate analyses showed that marital status was associated with pessimism ($p = 0.019$), and educational level and marital status were associated with depression ($p = 0.049$, and $p = 0.004$, respectively); see Table 2.

Table 1
Distribution of sociodemographic and clinical characteristics in the study population (n = 240).

Characteristics	Number of patients	%
Age		
≤ 65 years	201	83.8
> 65 years	39	16.3
Educational level		
Primary	187	77.9
High school or above	53	22.1
Marital Status		
Married/partnered	172	71.7
Not partnered	68	28.3
Employed		
No	106	44.2
Yes	134	55.8
Body Mass Index		
BMI <24.9	121	50.4
BMI ≥ 25	119	49.6
Stage		
I–II	214	89.2
III	26	10.8
Treatment		
Chemotherapy	81	33.8
Chemo- and radiotherapy	159	66.3
Comorbidities		
No	183	76.3
Yes	57	23.8

Table 2
Distribution of socio-demographic and clinical characteristics in subgroups with different symptoms (pessimism, depression, fatigue, and pain) (n = 240).

Characteristics	Pessimism	Depression	Fatigue	Nausea	Pain
Age %					
≤65 years	25.0	37.8	9.0	2.0	3.5
>65 years	35.9	51.3	7.7	0.0	7.7
p value	.164	.116	.798	.374	.229
Educational level					
Primary	59.2	**43.3**	10.2	2.1	4.8
High school or above	57.0	**28.3**	3.8	0.0	1.9
p value	.213	**.049**	.146	.283	.347
Marital Status					
Married/partnered	**59.8**	**34.3**	8.1	2.3	4.1
Not partnered	**56.0**	**54.4**	10.3	0.0	4.4
p value	**.019**	**.004**	.595	.205	.905
Employed					
No	58.9	51.5	8.5	0.0	6.6
Yes	58.6	38.8	9.0	3.0	2.2
p value	.834	.671	.899	.073	.093
Body Mass Index					
BMI <24.9	57.6	41.3	7.4	2.5	2.5
BMI ≥25	59.7	38.1	10.2	0.8	5.9
p value	.141	.615	.456	.325	.183
Stage					
I–II	58.4	39.6	8.0	1.4	3.8
III	62.0	38.5	11.5	3.8	7.7
p value	.117	.909	.542	.363	.347
Treatment					
Chemotherapy	58.8	40.7	8.6	1.2	2.5
Chemo- and radiotherapy	58.7	39.6	8.8	1.9	5.0
p value	.923	.867	.966	.709	.348
Comorbidities					
No	58.7	38.8	8.7	1.6	3.8
Yes	58.8	43.9	8.8	1.8	5.3
p value	.964	.496	.995	.953	.635

3.3. Multivariate analysis of the factor related with functional HRQoL and global health status

The results of the correlation analysis indicated that pessimism was correlated with global health status, while depression, fatigue, and pain correlated with functional HRQoL and global health status; see Table 3.

The results of logistic regression analysis indicated that depression had a significant influence on HRQoL (physical, role, emotional, cognitive, and social functioning) and global health status. Depression, together with pain, had a significant effect on physical function (Nagelkerke's $R^2 = 16.8$), whereas depression, in conjunction with fatigue, had a significant effect on role function (Nagelkerke's $R^2 = 13.4$). Furthermore, depression, associated with fatigue and pain, significantly influenced cognitive function (Nagelkerke's $R^2 = 25.9$), while the combination of depression and pessimism, as well as fatigue had a significant effect on social function (Nagelkerke's $R^2 = 23.5$). Finally, depression had a significant effect on emotional function and global health status (Nagelkerke's $R^2 = 21.1$ and $R^2 = 26.9$, respectively); see Table 4.

4. Discussion

Our prospective study sheds light on the association between breast cancer patients' psychological status (depression and anxiety) and physical symptoms, such as fatigue and pain, on their functional status and global health status. Depression has proven to be the factor that exerts the strongest explanatory power in the five HRQoL domains (physical, role, cognitive, emotional, and social), and global health status. Fatigue had a significant effect on four of the five domains and pain on two of the five domains.

The prevalence rates of pessimism (23.3%) and depression (40.0%) were similar to those seen in prior studies involving individuals with breast cancer (16–46.8% and 8–54.5, respectively) [5,6,22]. The possible causes for this broad range of prevalence may be due to demographic variables, such as age, marital status, stage of the cancer, and type of treatment [5,16]. The presence of depressive symptoms in people with breast cancer negatively affects their wellbeing, social role, emotional status, and deteriorate their QoL [17,23]. This can impact tolerance to adjuvant chemotherapy, hindering treatment adherence, which, in turn can reduce survival rates [24]. Pessimism can predict how a person reacts to stressful situations and is related to psychological distress prior to surgery in patients with breast cancer [14]. The most pessimistic breast cancer survivors reported worse QoL, even years after surviving cancer, when compared to non-pessimistic women [15]. The prevalence of depression in our study was somewhat higher than in previous studies [5,6,22]. This discrepancy might be due to differences in the sample, cultural context, and, especially, in the definition of depression applied, the method followed, and timing of evaluation [25] (after participants' first visit to the medical oncologist). At this appointment, they were informed of the need to receive adjuvant chemotherapy, its characteristics and benefit in reducing the risk of recurrence of the cancer, as well as the side effects with changes in physical appearance (hair loss, weight gain due to premedication with steroids, dry skin, and skin lesions) and in their general status, with frequent asthenia. Consequently, uncertainty surrounding prognosis and side effects in patients who are about to undergo adjuvant chemotherapy can be a source of major psychological distress [26].

Fatigue is one of the most common and stressful symptoms expressed by patients with breast cancer and was the physical symptom with the greatest explanatory power in four of the five HRQoL domains (physical, role, cognitive, and social function) in this series. On the other hand, pain was associated with physical and cognitive function. These results are in line with prior studies, that revealed fatigue and pain to be negative predictors of HRQoL in patients with breast cancer [10,27,28]. The prevalence of fatigue and pain in our sample before initiating adjuvant chemotherapy

Table 3
Univariate analysis of correlation among clinical variables and quality-of-life domains.

Variable	Physical Function	Role Function	Cognitive Function	Emotional Function	Social Function	Global Health
Pessimism	.017	-.119	.099	-.096	-.124	.201**
Depression	-.290**	-.288**	-.689**	-.354**	-.439**	-.455**
Fatigue	-.492**	-.591**	-.423**	-.559**	-.591**	-.478**
Nausea and vomiting	-.258**	-.359**	-.190**	-.363**	-.290**	-.345**
Pain	-.424**	-.508**	-.243**	-.374**	-.501**	-.338**
Mean	87.4	75.9	68.9	82.9	75.4	70.2
Standard Deviation	14.0	25.9	26.7	20.9	25.4	20.3

*$p < 0.01$ (two-tailed); **$p < 0.001$ (two-tailed).

Table 4
Multivariate logistic regression of factors correlated with functional (physical, role, cognitive, emotional, social) domains of quality of life and global health status.

Variable	β	Wald test (z-ratio)	Odds ratio	95% CI	β	Wald test (z-ratio)	Odds ratio	95% CI
		Physical Function				Role Function		
Pessimism	–	–	–	–	–	–	–	–
Depression	−1.337	15.218**	.263	.13−.51	-.876	9.749*	.002	.24−.72
Fatigue	–	–	–	–	−1.810	7.757*	.005	.04−.58
Nausea	–	–	–	–	–	–	–	–
Pain	−2.067	7.752*	.127	.03−.54	–	–	–	–
		Cognitive Function				Emotional Function		
Pessimism	–	–	–	–	–	–	–	–
Depression	-.872	7.814**	.418	.22−.77	−1.849	35.090**	.157	.09−.29
Fatigue	−2.751	12.492**	.068	.01−.29	–	–	–	–
Nausea	–	–	–	–	–	–	–	–
Pain	−2.256	4.042*	.105	.01−.94	–	–	–	–
		Social Function				Global Health Status		
Pessimism	-.731	4.236*	.481	.24−.96	–	–	–	–
Depression	−1.276	18.376**	.279	.17−.50	−1.618	25.736**	.198	.11−.37
Fatigue	−3.074	8.472*	.046	.01−.37	–	–	–	–
Nausea	–	–	–	–	–	–	–	–
Pain	–	–	–	–	–	–	–	–

*Adjusted for demographic and clinical variables (age, education, marriage, work, BMI, cancer stage, comorbidities and treatment).
*$p < 0.01$ (two-tailed); **$p < 0.001$ (two-tailed).

was 8.8% and 4.2%, respectively, lower than results in patients at treatment completion, which tends to be 40%−80% [27] and 16%−20%, respectively [29]. Fatigue usually appears together with other symptoms, such as pain, sleep disturbances, or depression [10,29,30]. The impact of fatigue on patients' QoL can be substantial, decreasing their engagement at work and participation in their social, family, and personal lives [10,30,31]. The women who experience more fatigue, sleep disturbances, and depression prior to initiating chemotherapy are also the ones who display greater fatigue and worse QoL during treatment [32]. This suggests that fatigue and pain are not only the result of chemotherapy or radiotherapy, but that their cause is multifactorial [32].

Depression was the number one factor accounting for participants' functional status. These results are similar to those that indicate that patients with depression have worse QoL [5,6,11] and worse functional status (physical, emotional, and social) than those without depression [6]. Untreated depression interferes with personal and sexual relations and with rehabilitation; while diminishing the patient's ability to cope with the disease and their QoL [11]. These findings provide evidence that psychological symptoms can have profound effects on patients' psychosocial wellbeing during cancer treatment. The results also prove that physical symptoms, such as fatigue and pain, also impact patients' functional status, albeit less so than psychological symptoms in the sample of patients studied that had not yet begun chemotherapy. There are studies that suggest that the physical symptoms, such as fatigue and pain, experienced by patients after completing treatment can persist for months and even years [30,31].

4.1. Limitations

The cross-sectional design of this study yielded information regarding the prevalence of psychological and physical symptoms at a given timepoint, after tumor resection and prior to adjuvant chemotherapy. The pattern and intensity of symptoms over time were not explored. Future research should also capture data as to the prevalence of these symptoms once adjuvant chemotherapy has been completed to evaluate the risk of persistence/chronification and their social repercussions. The measures used to examine psychological (pessimism and depression) and physical (fatigue and pain) symptoms are not a substitute for a diagnosis based on a structured clinical interview. That being said, an intensive and expensive evaluation by means of interviews would not be viable, given the cost in terms of time and personnel, as well as the more than likely decrease of patient participation in the study.

4.2. Clinical implications

Psychological and physical symptoms have a detrimental effect on breast cancer patients' functional status and QoL. Some authors suggest that psychological symptoms can decrease the efficacy of chemotherapy and tolerance in patients with breast cancer [6]. It is important to incorporate measures to assess pessimism and depression in medical procedures. Once psychological symptoms are detected, patients can be referred to the psycho-oncologist for help in accepting and confronting their cancer. The results can also

help nurses and medical oncologists to better support their patients with breast cancer who are at risk for presenting psychological symptoms during treatment. For instance, they can adapt the information they provide to prepare patients more effectively for treatment; they can evaluate them regularly, and teach them strategies to relieve the symptoms that have such a deleterious effect on their QoL and functionality.

Conflict of interest

All authors declare that they have no conflict of interest. This is an academic study.

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Ethical statement

The study has been performed in accordance with the ethical standards of the Declaration of Helsinki and its subsequent amendments. This study is an observational trial without intervention.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2019.01.012.

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