Original Article

Eur J Breast Health 2019; 15(1): 26-31
DOI: 10.5152/ejbh.2018.4297

Advanced Clinical Stage at Diagnosis of Breast Cancer Is Associated with Poorer Health-Related Quality of Life: A Cross-Sectional Study

Julia de Mello Ramirez Medina[1], Ingrid de Araujo Trugilho[1], Giovanna Nunes Belo Mendes[2], Josiel Guedes Silva[3], Maria Alexsandra da Silva Paiva[4], Suzana Sales de Aguiar[1], Luiz Claudio Santos Thuler[1], Anke Bergmann[1]

[1]Department of Clinical Epidemiology, National Cancer Institute, Rio de Janeiro, Brazil
[2]CEUMA University, Maranhão, Brazil
[3]Federal University of Maranhão, Maranhão, Brazil
[4]Estácio College of Amazonas, Manaus, Brazil

ABSTRACT

Objective: To describe the clinical stage in women diagnosed with breast cancer and the association between clinical stage and Health-related quality of life (HRQoL).

Materials and Methods: This was a cross-sectional study involving women diagnosed with breast cancer. HRQoL was assessed with European Organization for Research and Treatment of Cancer 30-Item Quality of Life Questionnaire and the Quality of Life Questionnaire Breast Cancer 23. The principal exposure was clinical stage (<IIB versus ≥IIB). Simple linear regression was performed and variables with $p<0.20$ were selected for the multiple linear regression. The final model was composed of statistically significant variables ($p<0.05$).

Results: In total, 302 women were included. The majority (58.9%) had been diagnosed with advanced stage cancer (≥IIB). Those at an advanced clinical stage had poorer role functioning ($p=0.029$), pain ($p<0.001$), and symptoms in the breast ($p<0.001$).

Conclusion: Advanced clinical stage at diagnosis was found to be associated with worse health-related quality of life in breast cancer patients.

Keywords: Breast neoplasm, quality of life, neoplasm staging

Cite this article as: Ramirez Medina JM, Trugilho IA, Belo Mendes GN, Guedes Silva J, Silva Paiva MA, Sales de Aguiar S, Santos Thuler LC, Bergmann A. Advanced Clinical Stage at Diagnosis of Breast Cancer Is Associated with Poorer Health-Related Quality of Life: A Cross-Sectional Study. Eur J Breast Health 2019; 15(1): 26-31.

Introduction

Breast cancer is one of the main causes of morbimortality among women worldwide, with approximately 1.67 million new cases and 522,000 deaths in 2012 (1). Breast cancer is the second most common cause of cancer-related death in developed countries and the first in developing countries (2). In Brazil in 2017, there were an estimated 57,960 new cases of breast cancer, with an incidence of 56.20 cases per 100,000 women, indicating that breast cancer is an important public health problem (3).

Given that it is a heterogenous and multi-factorial disease, the evolution of breast neoplasm involves important biopsychosocial factors that directly interfere with the quality of life of affected women (4). Health-related quality of life (HRQoL) assessment has been used for evaluating the impact of the disease on the patient, for preparing indicators of the severity and progression of the disease and for predicting the influence of treatments on the individual's perception of their position in life (5).

Health-related quality of life means that the expression "being healthy" is no longer understood as simply an absence of disease; rather, it is seen as a state reflecting mental, physical and social well-being (6). In this context, the concept of HRQoL refers to the value that can be placed on life due to the modifications that may occur because of diseases or conditions, treatments and health care policies (7).

Questionnaires that evaluate HRQoL have been widely used in clinical research. Generic instruments are used for various health conditions and allow comparisons to be made, while specific instruments are more sensitive and enable evaluation of a specific condition, such as breast cancer. Quantitative measures of HRQoL facilitate recognition of functional and emotional problems that are not always detected in conventional clinical evaluation, providing better monitoring and communication between patients and the health team (5-10).

Considering individual perceptions of HRQoL, it is essential to understand the main altered factors at the time of breast cancer diagnosis (8). In this context, the results of this study can increase scientific knowledge and provide insight into appropriate supportive actions, with

Corresponding Author:
Anke Bergmann; abergmann@inca.gov.br

Submitted: 07.08.2018
Accepted: 12.10.2018
Available Online Date: 19.12.2018

the aim of improving HRQoL in women with breast cancer. Thus, the aim of this study was to evaluate the impact of clinical stage (initial x advanced) on HRQoL in women diagnosed with breast cancer.

Material and Methods

This is an analytical cross-sectional study involving women diagnosed with breast cancer. It was performed at the Cancer Hospital III of the Brazilian National Cancer Institute (HCIII, INCA), Rio de Janeiro, Brazil, between April and December 2016.

Adult women (over 18 years) who had recently been diagnosed with breast cancer and who had signed the informed consent form were included in the study. Participants were excluded if they had previously undergone oncological treatment, did not have clinical or oncological conditions requiring surgical treatment, had altered gait or difficulty walking, had visual or hearing impairment that would affect completion of the questionnaires, had a prior history of cancer, were not clinically or psychologically able to answer to the questionnaire, or were participating in clinical research trials.

Patients were recruited at their first appointment at the Clinical Oncology Service or on the day before their surgical procedure. Those who agreed to participate in the study were asked to sign the informed consent form and were interviewed by a team of previously trained researchers.

The data were obtained through interview and active search of physical and electronic records. The socio-demographic and clinical variables collected were: age, schooling (years of study), self-declared skin colour, location of residence, occupation, marital status, household income per capita (it was calculated by dividing the family´s total income by the total number of members of the family that depend on this income), comorbidities (Charlson comorbidity index), presence of systemic arterial hypertension, alcohol (report of alcohol consumption, at any intensity, in the 30 days prior to the interview) and tobacco (current consumption, in any quantity), clinical stage (<IIB or ≥IIB) and proposed treatment (neoadjuvant chemotherapy or surgery). The outcome investigated was quality of life as assessed with the European Organization for Research and Treatment of Cancer 30-Item Quality of Life Questionnaire (EORTC QLQ-30) and the Quality of Life Questionnaire Breast Cancer 23 (QLQ-BR23), both translated and validated in Portuguese (10).

The EORTC QLQ-C30 is a 30-item questionnaire that includes five functional scales (physical, role, cognitive, emotional and social), symptom scales (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties) and global health status. The scores range from 0 to 100, with 0 representing the worst state of health and 100 the best, with the exception of symptoms scales in which a higher score represents more symptoms and worse quality of life (10).

The EORTC QLQ-BR23 is a supplementary questionnaire specifically for breast cancer patients (10). This questionnaire has 23 questions, divided into two dimensions: functional scale (body image, sexual functioning, sexual enjoyment and future perspective) and symptom scale (systemic therapy side effects, breast symptoms, arm symptoms and upset by hair loss). In this study, effects of systemic therapy and being upset by hair loss were not included, as our evaluation was performed at the time of breast cancer diagnosis. Furthermore, the sexual satisfaction dimension was not analysed because less than 50% of responses were obtained.

The scores for the EORTC QLQ C-30 and EORTC QLQ-BR23 were calculated in accordance with the EORTC manual (11). Descriptive analysis included means and standard deviations for the continuous variables and distribution of absolute and relative frequencies for the categorical variables. Student's t-test was used to compare the means of the quality of life scores according to clinical staging at diagnosis. P values <0.05 were considered statistically significant. To evaluate the outcome (HRQoL), simple linear regression was carried out; variables with p<0.20 were selected for the multiple regression analysis. The final model included only the statistically significant variables (p<0.05). The statistical analysis was undertaken using IBM Statistical Package for Social Sciences (SPSS), version 20.0 (IBM Corp.; Armonk, NY, USA).

This study was approved by the research ethics committee of the José Alencar Gomes da Silva National Cancer Institute (INCA), record number 1.400.320, in accordance with the National Health Council Resolution No.466/12, which provides guidelines and regulatory norms for research involving human beings.

Results

In total, 302 women were interviewed; the mean age of participants was 53.7 years (SD±11.9 years). Most women had ≥8 years of schooling (66.6%), were married or with stable union (50.3%), worked (46.7%), had a per capita income of ≤1 minimum monthly wage (58.9%) and lived in the city of Rio de Janeiro (53.6%). Regarding behavioural habits, 28.1% of patients reported alcohol consumption and 10.9% used tobacco (Table 1).

Regarding the clinical variables, 58.9% had advanced stage cancer (≥IIB), and the most frequently proposed treatment was neoadjuvant chemotherapy (64.6%). Most women had no comorbidities (83.1%) and no systemic arterial hypertension (66.0%) (Table 2).

In terms of evaluation of HRQoL using the EORTC QLQ-C30, the worst score was observed for emotional functioning (mean 58.9±30.6) and the best score was for physical functioning (mean 83.4±19.3). For the symptom scales, the worst scores were reported for insomnia (mean 36.1±41.1), followed by pain (mean 32.1±32.9) and fatigue (mean 21.8±24.3).

The best scores on the EORTC QLQ-BR-23 were obtained for body image (mean 83.4±25.1), while breast symptoms were more common than arm symptoms, with means of 29.4±28.9 and 18.1±23.5, respectively (Table 3).

Comparison of the means of different HRQoL functions according to the clinical stage of breast cancer revealed that patients in the early stages had better role functioning than those in advanced stages (p=0.04). Of the symptoms, pain was more commonly reported by patients in advanced stages than in early stages (p<0.001). Breast symptoms were also more frequent in advanced stage patients compared to those in early stages (p<0.001) (Table 3).

The univariate analysis of the variables associated with the HRQoL domains (role functioning, pain and breast symptoms) are presented in Supplementary Table 1.

The adjusted analysis showed that patients in advanced stages had worse role functioning (p=0.029, adjusted for occupation and educational level), pain (p<0.001, adjusted for age, occupation and marital

Table 1. Sociodemographic and epidemiological characteristics (N=302)

Variables	N	%
Age		
Mean (±SD)	53.7 (±11.9)	
Race/ skin color*		
Mulatto	136	45.0
White	103	34.1
Black	57	18.9
Asian Brazilians and indigenous	5	1.7
Missing	1	0.3
Educational level (years)		
≥8 years	201	66.6
0 to 7 years	100	33.1
Missing	1	0.3
Occupation		
Working	141	46.7
Not working	140	46.4
Illness benefits	12	4.0
Missing	9	3.0
Alcohol consumption (30 days)		
No	209	69.2
Yes	85	28.1
Missing	8	2.6
Smoking		
No	260	86.1
Yes	33	10.9
Missing	9	3.0
Per capita income**		
≤1 minimum wage	178	58.9
>1 minimum wage	111	36.8
Missing	13	4.3
Marital status		
Married or stable union	152	50.3
No partner	149	49.3
Missing	1	0.3
Place of residence		
Rio de Janeiro city	162	53.6
Metropolitan region	130	43.0
Other	10	3.3

*According to the Brazilian Institute of Geography and Statistics (IBGE)
**At the time of this study, 1 monthly minimum wage was R$ 880.00 (equivalent to U$ 252.14 on April 04th, 2016)

Table 2. Clinical and tumor characteristics (N=302)

Variables	N	%
Clinical staging		
<IIB	113	37.4
≥IIB	178	58.9
Missing	11	3.6
Proposed treatment		
Surgery	107	35.4
Neoadjuvant chemotherapy	195	64.6
Comorbidity		
No	251	83.1
Yes	49	16.2
Missing	2	0.7
Arterial hypertension		
No	169	56.0
Yes	133	44.0

status) and breast symptoms (p<0.001, adjusted for age and occupation) when compared to those in early stages (Table 4).

Discussion and Conclusion

In this study of 302 women diagnosed with breast cancer, 58.9% of the participants were at an advanced clinical stage, and this clinical stage was associated with poorer quality of life in terms of role functioning, pain and breast symptoms.

Consistent with the current study, Abrahão et al. (12) found that, in Brazil, the majority of breast cancer cases (53.5%) were diagnosed at stage ≥IIB. Another Brazilian study reported that 51% of patients were diagnosed at advanced stage (from II to IV) (13). This is in contrast with North American data, showing that 40-44% of women were diagnosed at stages II to IV (14, 15).

In the current study, patients in advanced stages had worse role functioning, even after adjusting for occupation and educational level (p=0.029). In a study conducted in Turkey, role functioning, as well as other HRQoL scores, were found to be affected after breast cancer diagnosis (16). This corroborates our results. Other dimensions of HRQoL have been shown to be affected by the discovery of cancer, including physical and social functions (17); although, in the current study, there were no associations between these functions and clinical stage at diagnosis. This disparity may be related both to methodological issues and demographic and clinical characteristics of the study populations.

With regards to the symptoms scale of the EORTC QLQ-C30, one of the main symptoms reported by our patients was pain, with worse scores at advanced stages when compared with early stages. Ganesh et al. (18) analysed 223 women with stage I and II breast cancer in Malaysia and also found pain to be the predominant symptom, with higher scores at clinical stage II (p=0.001). The study by Goudas et al. (19) found that one-quarter of patients with breast cancer have

Table 3. Comparison between quality of life scores according to clinical stage (n=302)

		Staging		
	Mean (±SD)	<IIB Mean (±SD)	≥IIB Mean (±SD)	p*
EORTC QLQ C-30				
Functional scales				
Physical functioning	83.4 (19.3)	84.4 (20.5)	82.8 (18.6)	0.49
Role functioning	76.1 (31.6)	80.9 (28.9)	73.1 (32.9)	0.04
Cognitive functioning	75.8 (26.6)	76.4 (26.9)	75.5 (26.5)	0.80
Emotional functioning	58.9 (30.6)	62.3 (31.6)	56.9 (29.9)	0.14
Social functioning	82.4 (29.4)	85.3 (27.2)	80.6 (30.6)	0.18
Symptom scales				
Fatigue	21.8 (24.3)	18.6 (23.4)	23.9 (24.7)	0.07
Pain	32.1 (32.9)	21.1 (29.4)	39.0 (33.1)	<0.001
Dyspnoea	10.9 (24.4)	10.3 (25.2)	11.2 (24)	0.76
Insomnia	36.1 (41.1)	32.4 (41.4)	38.4 (40.8)	0.23
Appetite loss	10.6 (24.5)	8.5 (22.2)	12.0 (25.9)	0.25
Nausea and vomiting	7.4 (15.5)	6.9 (14.7)	7.7 (16.1)	0.69
Constipation	17.7 (31.6)	20.1 (34.7)	16.3 (29.4)	0.32
Diarrhoea	5.9 (17.8)	6.8 (20.4)	5.4 (15.9)	0.52
Financial Difficulties	29.5 (41.3)	31.0 (41.9)	28.6 (40.9)	0.64
Global health status	70.5 (22.8)	72.0 (23)	69.6 (22.8)	0.40
EORTC BR-23				
Functional scales				
Body image	83.4 (25.1)	83.9 (26.3)	83.1 (24.4)	0.80
Sexual functioning	34.1 (31.7)	32.1 (31.5)	35.3 (31.9)	0.41
Future perspective	36.3 (39.2)	38.3 (39.2)	35.0 (39.3)	0.48
Symptom scales				
Breast symptoms	29.4 (28.9)	14.8 (18.3)	38.8 (30.6)	<0.001
Arm symptoms	18.1 (23.5)	15.2 (21.7)	19.9 (24.4)	0.10

*In bold statistically significant p values
EORTC QLQ-30: European Organization for Research and Treatment of Cancer 30-Item Quality of Life Questionnaire; QLQ-BR23: Quality of Life Questionnaire Breast Cancer 23; SD: standard deviation

oncological pain at diagnosis, one-third have pain during treatment and three-quarters have pain at advanced clinical stages. In this study, the symptoms scale of the EORTC QLQ-BR-23 questionnaire also showed worse scores for breast symptoms among those at clinical stage ≥IIB. In a sample of 549 women, Aguiar et al. (4) also found that breast symptoms were a significant psycho-emotional component influencing quality of life in breast cancer survivors.

According to King et al. (17), when cancer diagnosis occurs in the early stages, physical, role and emotional function measures of quality of life are not changed. The impact of diagnosis on HRQoL is predominantly psychological, differing from the impact of treatment, which has both physical and psychological impacts. In the pilot study by Gavric et al. (20) involving 100 women, the worst scores on the EORTC QLQ-C30 functional scales were observed for emotional functioning (p<0.001).

The current study did not find an association between emotional functioning and clinical stage at breast cancer diagnosis. Cancer-related insomnia has been widely linked with depression, pain and fatigue (21). In another study, anxiety, pain, clinical stage, type of treatment proposed and lumbar pain explained 51.2% of breast cancer-related cases of insomnia (22).

In this study, the sexual satisfaction dimension was not analysed due to high missing rates (>50%), because more than 50% of the answers were not obtained. In a cross-sectional study with Spanish women after breast cancer treatment, 91% related some sexual dysfunction

Table 4. Multiple analysis of the advanced stage associated with the HRQoL domains (Role functioning, Pain and Breast symptoms) (n=302)

	≥IIB x <IIB		
Variables	**Beta**	**95%IC**	**p***
Role functioning[a]	-8.30	-15.76 to -0.85	0.029
Pain	15.91	7.09 to 22.53	<0.001
Breast symptoms	19.97	13.73 to 26.20	<0.001

*Statistically significant p values in bold
[a]Adjusted by occupation and educational level
[b]Adjusted by age, occupation, marital status
[c]Adjusted by age and occupation

due to penetration pain (50.6%), lubrication (50.6%), dysfunctional desire (44.6%) and dysfunctional excitement (44.6%) (23). We can speculate that the high prevalence of sexual dysfunction may explain the lack of response on sexual satisfaction in our study.

The main limitation of this study is that the findings may not be generalisable to other populations with different socio-demographic and clinical characteristics. In addition, although HRQoL measurements were more appropriate after breast cancer treatments, we chose to measure HRQoL before the beginning of the treatment to assess the impact of the initial clinical stage on HRQoL. This fact may have introduced measurement bias.

A strength of the current study is that it investigated quality of life at the time of breast cancer diagnosis, enabling appropriate post-treatment follow-up of the patients. Furthermore, this is, to our knowledge, the first study to compare HRQoL of women in early and advanced stages of the disease at the time of their breast cancer diagnosis.

In conclusion, this study found that patients with advanced stage breast cancer at the time of diagnosis reported poorer role functioning, pain and breast symptoms when compared to patients at an early stage of the disease. The perception of pain was found to be the main symptom that affected quality of life.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of the José Alencar Gomes da Silva National Cancer Institute (INCA) (1.400.320).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.S.A., L.C.S.T., A.B.; Design - J.M.R.M., I.A.T.; Supervision - S.S.A.; Data Collection and/or Processing - G.N.B.M., J.G.S., M.A.S.P.; Analysis and/or Interpretation - S.S.A., L.C.S.T., A.B., G.N.B.M., J.G.S., M.A.S.P., J.M.R.M., I.A.T.; Literature Search - G.N.B.M., J.G.S., M.A.S.P.; Writing Manuscript - S.S.A., L.C.S.T., A.B., G.N.B.M., J.G.S., M.A.S.P., J.M.R.M., I.A.T.; Critical Review - S.S.A., L.C.S.T., A.B., G.N.B.M., J.G.S., M.A.S.P., J.M.R.M., I.A.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. International Agency For Research On Cancer. (2014). World Cancer Report 2014. World Health Organization. Available from: http://www.who.int/cancer/publications/WRC_2014/en/ (cited 2018 June 1).
2. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN. v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr (cited 2018 June 12).
3. Instituto Nacional de Câncer José Alencar Gomes da Silva (2015). Ministério da saúde. Estimativas 2016: Incidência De Câncer No Brasil, Brasil. Available from: http://www.inca.gov.br/estimativa/2018/ (cited 2018 May 8).
4. De Aguiar SS, Bergmann A, Mattos IE. Quality of life as a predictor of overall survival after breast cancer treatment. Qual Life Res 2014; 23: 627-637. (PMID: 23873516) [CrossRef]
5. WHOQOL Group. The development of the World Health Organization quality of life assessment instrument (the WHOQOL). In: Orley, J.; Kuyken, W. (Eds.). Quality of life assessment: international perspectives. Heidelberg: Springer, 1994. [CrossRef]
6. The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. Soc Sci Med 1998; 46: 1569-1585. (PMID: 9672396) [CrossRef]
7. Azuero A, Su X, McNees P, Meneses K. A revision of the quality of life-breast cancer survivors (QOL-BCS) instrument. Res Nurs Health 2013; 36: 423-434. (PMID: 23512217) [CrossRef]
8. Lee CK, Hudson M, Simes J, Ribi K, Bernhard J, Coates AS. When do patient reported quality of life indicators become prognostic in breast cancer? Health Qual Life Outcomes 2018; 16: 13. (PMID: 29329582) [CrossRef]
9. Rautalin M, Färkkilä N, Sintonen H, Saarto T, Taari K, Jahkola T, Roine RP. Health-related quality of life in different states of breast cancer – comparing different instruments. Acta Oncol 2018; 57: 622-628. (PMID: 29140139) [CrossRef]
10. Michels FA, Latorre MR, Maciel MS. Validity, reliability and understanding of the EORTC-C30 and EORTC-BR23, quality of life questionnaires specific for breast cancer. Rev Bras Epidemiol 2013; 16: 352-363. (PMID: 24142007) [CrossRef]
11. Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. On behalf of the EORTC Quality of Life Group. EORTC QLQ-C30 Scoring Manual (3rd edition). Brussels: EORTC; 2001.
12. Abrahão KS, Bergmann A, Aguiar SS, Thuler LC. Determinants of advanced stage presentation of breast cancer in 87,969 Brazilian women. Maturitas 2015; 82: 365-370. (PMID: 26358931) [CrossRef]
13. Rezende MC, Koch HA, Figueiredo JA, Thuler LC. Factors leading to delay in obtaining definitive diagnosis of suspicious lesions for breast cancer in a dedicated health unit in Rio de Janeiro. Rev Bras Ginecol Obstet 2009; 31: 75-81. (PMID: 19407912)
14. Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner MJ. SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001. Available from: https://seer.cancer.gov/archive/publications/survival/ (cited 2018 May 8).
15. Davidson A, Chia S, Olson R, Nichol A, Speers C, Coldman AJ, Bajdik C, Woods R, Tyldesley S. Stage, treatment and outcomes for patients with breast cancer in British Columbia in 2002: a population-based cohort study. CMAJ Open 2013; 1: 134-141. (PMID: 25077115) [CrossRef]
16. Gokgoz S, Sadikoglu G, Paksoy E, Guneytepe U, Ozcakir A, Bayram N, Bilgel NG. Health Related Quality of Life among Breast Cancer Patients: a Study from Turkey. Glob J Health Sci 2012; 3: 140-152.
17. King MT, Winters ZE, Olivotto IA, Spillane AJ, Chua BH, Saunders C, Westenberg AHG, Mann B, Burnett P, Butow P, Rutherford C. Patient-reported outcomes in ductal carcinoma in situ: A systematic review. Eur J Cancer 2017; 71: 95-108. (PMID: 27987454) [CrossRef]

18. Ganesh S, Lye MS, Lau FN. Quality of Life among Breast Cancer Patients in Malaysia. Asian Pac J Cancer Prev 2016; 17: 1677-1684. (PMID: 27221837) [CrossRef]
19. Goudas LC, Bloch R, Gialeli-Goudas M, Lau J, Carr DB. The epidemiology of cancer pain. Cancer Invest 2005; 23: 182-190. (PMID: 15813511) [CrossRef]
20. Gavric Z, Vukovic-Kostic Z. Assessment of quality of life of women with breast cancer. Glob J Health Sci 2016; 8: 1-9. (PMID: 27157152) [CrossRef]
21. Davis MP, Khoshknabi D, Walsh D, Lagman R, Platt A. Insomnia in patients with advanced cancer. Am J Hosp Palliat Care 2014; 31: 365-373. (PMID: 23616275) [CrossRef]
22. Galiano-Castillo N, Arroyo-Morales M, Ariza-Garcia A, Fernández-Lao C, Fernández-Fernández AJ, Cantarero-Villanueva I. Factors that Explain the Cancer-Related Insomnia. Breast J 2017; 23: 387-394. (PMID: 28117498) [CrossRef]
23. Cobo-Cuenca AI, Martín-Espinosa NM, Sampietro-Crespo A, Rodríguez-Borrego MA, Carmona-Torres JM. Sexual dysfunction in Spanish women with breast cancer. PLoS One 2018; 13: e0203151. (PMID: 30169506) [CrossRef]