

Influence of pain on the functionality of the upper limbs in breast cancer survivors: a post-operative analysis at 6 and 12 months

Influência da dor na funcionalidade dos membros superiores em sobreviventes de câncer de mama: uma análise pós-operatória a 6 e 12 meses

DOI:10.34119/bjhrv4n6-306

Recebimento dos originais: 18/10/2021

Aceitação para publicação: 12/11/2021

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ABSTRACT

Introduction: Breast cancer is the most common cancer in women, and the various procedures and treatments performed after diagnosis can trigger physical symptoms. The objective was to verify the influence of pain on the functionality of the upper limbs (UL) in women after breast cancer surgery, in two postoperative periods. *Methods:* This is an exploratory cross-sectional study with women evaluated postoperatively at 6 (N=126) and 12 months (N=74). The outcomes were assessed using a Pain Body Diagram, a Numerical Pain Scale, and Quick-DASH. Multiple linear hierarchical regression analysis was performed adjusting for pain, clinical (radiotherapy, chemotherapy and axillary intervention), and sociodemographic variables (age, education level, ethnic), $p < 0.05$. *Results:* Participants in the 6-month group had a similar functionality score (mean=27, SD=18.9) compared to the 12-month group (mean=24.6, SD=19.1). In both postoperative periods, the intensity of pain was classified as moderate, and the anterior region of the trunk was the most affected. Pain was more prevalent at 6 months (71.4%) compared to 12 months PO (57.3%), but the intensity of pain in the anterior and lateral trunk for the 12 months PO group was significantly higher compared to those at 6 months PO ($p < 0.05$). Among the variables included in the model, only pain was associated with worse functionality scores both at 6 ($R^2=0.23$) and at 12 months postoperatively ($R^2=0.31$). *Conclusion:* Pain was the most important factor influencing upper limb functionality. These results can guide professionals to foster pain control strategies to improve upper limb functionality.

Keywords: Breast Cancer; Pain; Functioning; Arm Morbidities; Upper Limb;

RESUMO

Introdução: O câncer de mama é a neoplasia mais comum em mulheres, e os diferentes procedimentos e tratamentos realizados após o diagnóstico podem desencadear sintomas físicos. O objetivo foi verificar a influência da dor na funcionalidade de membros superiores (MS) em mulheres após cirurgia de câncer de mama, em dois pós-operatórios. *Métodos:* Trata-se de um estudo transversal exploratório com mulheres avaliadas no pós-operatório com 6 (N = 126) e 12 meses (N = 74). Os resultados foram avaliados por meio de um diagrama corporal da dor, uma escala numérica de dor e o Quick-DASH. Foi realizada análise de regressão linear múltipla, ajustando para dor, variáveis clínicas (radioterapia, quimioterapia e intervenção axilar) e sociodemográficas (idade, escolaridade, etnia), $p < 0,05$. *Resultados:* Os participantes do grupo de 6 meses tiveram uma pontuação de funcionalidade semelhante (média = 27, DP = 18,9) em comparação

com o grupo de 12 meses (média = 24,6, DP = 19,1). Em ambos os períodos de pós-operatório, a intensidade da dor foi classificada como moderada, sendo a região anterior do tronco a mais acometida. A dor foi mais prevalente em 6 meses (71,4%) em comparação com 12 meses PO (57,3%), mas a intensidade da dor no tronco anterior e lateral para o grupo PO 12 meses foi significativamente maior em comparação com aqueles em 6 meses PO ($p < 0,05$). Dentre as variáveis incluídas no modelo, apenas a dor se associou a piores escores de funcionalidade tanto no 6º ($R^2 = 0,23$) quanto no 12º mês de pós-operatório ($R^2 = 0,31$). Conclusão: A dor foi o fator mais importante para influenciar a funcionalidade do membro superior. Esses resultados podem orientar os profissionais a promover estratégias de controle da dor para melhorar a funcionalidade dos membros superiores.

Palavras-chave: Câncer de mama; Dor; Funcionalidade; Morbidades do braço; Membro superior;

1 INTRODUCTION

In global health statistics, breast cancer is the most common cancer in women [1]. Over the years, survival rates have progressed along with the advancement of treatments [2]. The main forms of treatment are chemotherapy, radiotherapy, hormone therapy, conservative surgical approach or mastectomy, and lymph node resection [2]. These treatments can trigger various physical symptoms such as pain, loss of functionality, and reduced range of motion, among others [2]. These complaints affect the active period of treatment and can endure, becoming chronic over time [3].

Pain is a common symptom in this population, with a prevalence of 25-60% [4], [1]. Generally, this pain manifests in the breast, in the upper limb homolateral to the surgery, in the lateral trunk, in the scapular waist, in the axillary region, and at the surgical incision [3], [5]. It is known that this symptom can appear in different postoperative periods (PO) [5]; however, there is little knowledge about the behavior of pain and its relationship with functionality over time.

Another characteristic observed in breast cancer survivors is decreased functionality [7], [8]. It is usually accompanied by factors such as fatigue, reduced range of motion, and loss of muscle strength [9], which can compromise the activities of daily living. This decreased functionality can also present itself from the initial postoperative period and persist over the years [8], [10]. Thus, the importance of early diagnosis is emphasized as a propellant for the prevention of the chronification of this symptom.

There is evidence that at 6 months after surgery, in most cases, women are still undergoing adjuvant treatment [11], and that their pain is a limiting factor in rehabilitation

in daily clinical practice [12]. On the other hand, after 12 months after surgery, pain can behave differently and still cause implications in the functionality of the upper limbs (UL) [8]. Specifically, in this postoperative period, a large part of the population has already returned to activities of daily life and/or work [13], where upper limb movement is an integral part of their multiple tasks. Thus, it is believed that there may be a relationship between pain and upper limb functionality at 6 and 12 months postoperatively, since the studies mostly focus their analyses on more recent or even late phases of the kinetic-functional rehabilitation process [8], [14].

The relevance of the present study for the interdisciplinary teams consists of verifying whether the high incidence of pain, identified didactically through mapping, maintains a relationship with the decreased functionality of the upper limbs when considering the intermediate and late phases of rehabilitation. This study can broaden the understanding of the behavior of these complaints, so that health professionals' interventions can prioritize the maintenance of health and safety and facilitate the return-to-work activities, without the chronification of the clinical-functional disabilities of the breast cancer survivors. The objective was to verify the influence of pain on the functionality of the upper limbs, at 6 and 12 months postoperatively, as well as identifying the intensity and location of pain.

2 MATERIALS AND METHODS

This was an exploratory cross-sectional study in two cuts, at 6 and 12 months PO. The present study was approved by the Ethics Committee on Research involving Human Beings of the Universidade do Estado de Santa Catarina (UDESC) under protocol numbers 2,835,766 and 3,613,485.

Participants

The participants were selected at three centers, in the periods from April 2018 to March 2019, in Florianópolis, Santa Catarina, Brazil. All women who met the inclusion criteria were contacted by telephone. The study included 200 women who had attended the breast oncology outpatient clinics of the previously mentioned hospitals. They were divided into two groups, one with 126 women who were in their 6th postoperative month, and the other with 74 women who were in their 12th postoperative month. All participants were women aged 18 and above who had been diagnosed with breast cancer and had

undergone breast surgery. The exclusion criteria consisted of cognitive alterations that would make it impossible to understand the instruments used, participation in rehabilitation follow-up in the 3 months prior to this study, self-reported psychiatric or psychological diseases, and functional limitations resulting from other diseases, such as strokes, fractures, or incapacitating orthopedic dysfunctions in the upper limbs.

Instruments

Socio-Demographic and Clinical Information

Information was collected from the medical records of the institutions regarding date of birth, contact telephone number, level of education, date of surgery, type of surgery, and surgical approach.

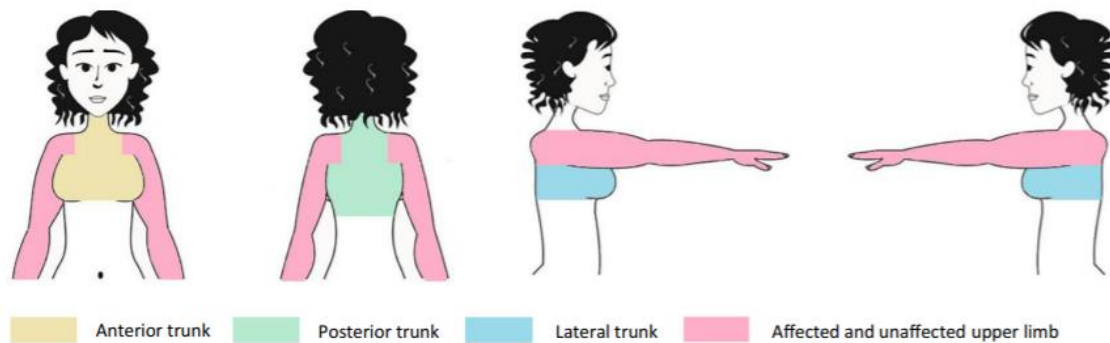
Functionality of the upper limbs

Functionality of the upper limbs was measured with Quick-DASH, which is a questionnaire derived from the Disability Questionnaire of the Arm, Shoulder and Hand (DASH) that is widely used to assess upper limb disability in breast cancer survivors. It was created in English [15] and later translated into the language of the participants [16] and serves as a quick way to evaluate the functionality of upper limbs during activities of daily living. It is composed of 11 questions that evaluate upper extremity disability and is an easy-to-understand functional assessment tool [17]. Its score ranges from 0 to 100, where a score closer to 100 indicates greater physical disability and symptoms in the upper limbs [16], [18].

Body Pain Diagram

The body pain diagram (Image 1) is a tool developed by the authors and has previously been used with breast cancer survivors [14] in a previous study [19]. It is a graphic representation of a woman's body in anterior, lateral, and posterior views, subdivided into body regions: anterior trunk, posterior trunk, lateral trunk, and upper limbs.

Image - 1



Visual Analogue Scale (VAS)

The visual analogue scale (VAS) is a numerical scale that helps to quantify symptoms, such as pain. It is easily understood and quickly applied. It offers a score from 0 to 10, in which 0 represents no pain at all and 10 represents extreme pain [20]. It is widely used in the breast cancer population [3], [8], and can be classified as “mild”, from 0 to 3, “moderate”, from 4 to 7, and “severe”, from 8 to 10 [21].

Data Collection Procedures

With the data from the socio-demographic and clinical records of these hospitals, women were contacted by telephone in order to compose the present sample. Upon reading and accepting the informed consent form, the participant was invited to join the study.

First, the participant was asked if she had experienced episodes of pain in the last seven days. If the answer was yes, the evaluator asked in which regions of the body the pain was present. According to the participant's report, the evaluator himself marked an X on the area identified as painful, following the legend of the Pain Body Diagram. After this step, the identification of the intensity of pain occurred in each location previously reported by the participant so she could refer to more than one area of involvement and different intensities of pain for each area. Finally, the 11 questions of the Quick-DASH instrument were applied.

3 STATISTICAL ANALYSIS

The data were organized in Excel (version 2010) and then analyzed using SPSS - Statistical Package for Social Sciences (version 20.0). For descriptive statistics, we used measures such as frequencies for categorical variables, mean and standard deviation for parametric data, and median and interquartile range for non-parametric data. The normality of the data was verified using the Kolmogorov-Smirnov test. Mann-Whitney's U test was used to compare the variables between the two groups for numerical variables and the chi-square test to compare proportions between the groups.

A multiple linear regression analysis was performed to identify the variables associated with upper limb functionality at 6 and 12 months postoperatively. To select the model to be included in the multiple linear analysis, a hierarchical model with three blocks was designed, based on the current literature on the subject. Block 1 included the clinical variables: axillary lymph node removal (0=no; 1=yes), radiotherapy and chemotherapy. Block 2 included socio-demographic variables: age (numeric), ethnicity (1=white; 2=non-white), and education level (1=up to 8 years of study; 2=more than 8 years). The last block introduced the variable presence of pain (0=no; 1=yes). The model was tested for the assumptions for regression analysis: Durbin Watson test for independence of errors, homoscedasticity and non-multi-collinearity (VIF). For power purposes, we set the 10 patients per independent variable included in the model as a minimum [28]. For multivariate analysis, logistic regression was performed in the enter method. The level of significance adopted was $p\text{-value} < 0.05$.

4 RESULTS

The clinical and sociodemographic characteristics are described in Table 1. The mean age of the group of women in the 6-month PO group was 55.46 ± 12.8 years, while it was 58.46 ± 12.8 years for the 12-month PO group.

Table 1 - Socio-demographic and clinical characteristics of the participants, at 6 and 12 months postoperatively, after breast cancer.

Variables	6 months PO (n=126)	12 months PO (n=74)	X^2	p
	n (%)	n (%)		
Marital Status			0.55	0.46
With partner	65 (52.1%)	34 (45.9%)		
No partner	61 (47.9%)	40 (54.1%)		
Schooling			4.61	0.03
< 8 years	66 (53%)	47 (68.1%)		
> 8 years	60 (47%)	27 (31.9%)		

Surgery side			0.00	0.99
Left	59 (46.8%)	34 (46.7%)		
Right	67 (53.2%)	40 (53.3%)		
Interventions				
Mastectomy	45 (36%)	28 (37.3%)	0.64	0.72
Conservative	79 (63.2%)	47 (62.7%)		
Axillary intervention	67 (59.8%)	31 (45.6%)	3.11	0.08
Lymph node biopsy	45 (40.2%)	37 (54.4%)	2.69	0.10
Radiotherapy				
Yes	65 (51.2%)	46 (62.5%)		
No	61 (48.8%)	28 (37.5%)	0.21	0.65
Chemotherapy				
Yes	87 (72.5%)	51 (69.9%)		
No	39 (27.5%)	23 (30.1%)	3.18	0.07
Hormonal therapy				
Yes	57 (46.9%)	44 (59.5%)		
No	69 (53.1%)	30 (40.5%)		

PO= postoperative period; N= frequency/number of participants

The data presented in Table 2 correspond to the frequency and intensity of pain in each body region. At 6 months postoperatively, the results indicate that 90 women (71.4%) reported pain in the last week, classified as moderate (vis: 4 to 7) with a mean intensity of 5.2. In the group corresponding to the 12-month postoperative period, 57.3% (n=43) reported pain in the last week, classified as moderate (NDE: 4 to 7) with a mean intensity of 6.68.

Table 2 - Comparison of the frequency and mean intensity of pain at 6 and 12 months after breast cancer mastectomy

	6 months PO (n=90)			12 months de PO (n=90)			p*
	Prevalence N (%)	Pain intensity Mean $\pm$ SD	Pain intensity MD(IR)	Prevalence N (%)	Pain intensity Mean $\pm$ SD	Pain intensity MD(IR)	
Anterior Trunk Pain	53 (42.1%)	5.24 $\pm$ 1.88	5 (3)	33 (44%)	6.50 $\pm$ 1.87	6.5 (30)	0.01
Posterior Trunk Pain	8 (6.3%)	5.12 $\pm$ 1.96	5 (3)	4 (5.3%)	7.33 $\pm$ 2.08	8 (0)	0.13
Lateral Trunk Pain	46 (36.5%)	5.21 $\pm$ 1.82	5 (3)	22 (29.3%)	6.47 $\pm$ 1.36	7 (3)	0.00
Pain homolateral upper limb	37 (29.4%)	5.86 $\pm$ 2.11	6 (4)	22 (29.3%)	6.09 $\pm$ 2.12	5 (4)	0.80
Pain contralateral upper limb	4 (3.2%)	4.50 $\pm$ 2.38	4.5 (5)	3 (4%)	7.00 $\pm$ 2.83	7 (0)	0.53

N= frequency/number of participants; SD=standard deviation; PO= postoperative; MD= median; IR=interquartile range * Mann Whitney U-test comparing pain intensity

The results of the Quick-DASH questionnaire showed that at 6 months after surgery the mean functionality score of the participants was 27.0 (SD=18.9; median=25). In the 12-month group, participants reached a mean of 24.6 (SD = 19.1, median = 23). There was no significant difference in upper extremity functionality between the 6- and 12-month PO groups (p=0.380).

After multiple linear regression with the variables introduced in the hierarchical model (clinical, sociodemographic, and pain variables), only the presence of pain was predictive of functionality both at 6 months ($R^2=0.23$) and at 12 months postoperatively ($R^2=0.31$) (Table 3). At 6 months postoperatively, the presence of pain was associated with an increase of 15.76 units in the upper extremity functionality score (DASH). Meanwhile, at 12 months postoperatively, the presence of pain was associated with an increase of 13.72 units in the functionality score.

Table 3 - Factors associated with upper limb functionality at 6 and 12 months following breast cancer surgery

Variables	6 months PO (n=90)					12 months PO (n=43)				
	B	SE B	β	R^2	p	B	SE B	β	R^2	p
Step 1 – Clinical				0.03					0.03	
Constant	28.20	3.31			0.00	29.03	4.48			0.00
Axillary intervention	-6.22	3.80	-0.17		0.10	-4.77	5.07	-0.13		0.35
Radiotherapy	1.91	3.74	0.05		0.61	-4.34	5.25	-0.11		0.41
Chemotherapy	0.36	4.22	0.01		0.93	-1.63	5.49	-0.04		0.77
Step 2 - Sociodemographic				0.10					0.19	
Constant	25.04	13.55			0.07	68.38	16.97			0.00
Axillary intervention	-5.01	3.78	-0.13		0.19	-3.59	4.89	-0.9		0.47
Radiotherapy	0.53	3.73	0.01		0.89	-4.68	4.99	-0.12		0.35
Chemotherapy	-1.85	4.30	-0.04		0.67	2.85	5.41	0.07		0.60
Education	-6.91	3.86	-0.19		0.08	-11.47	5.52	-0.27		0.04
Ethnicity	11.43	6.38	0.18		0.08	5.21	9.68	0.07		0.59
Age	0.02	0.16	0.02		0.87	-0.55	0.20	-0.37		0.01
Step 3 - Pain				0.23					0.31	
Constant	28.39	12.60			0.03	63.51	15.97			0.00
Axillary intervention	-5.73	3.51	-0.15		0.11	-1.89	4.61	-0.05		0.68
Radiotherapy	-0.93	3.48	-0.03		0.79	-3.98	4.68	-0.10		0.40
Chemotherapy	-2.13	3.99	-0.05		0.59	0.06	5.16	0.00		0.99
Education	-5.16	3.61	-0.14		0.16	-9.33	5.22	-0.22		0.08
Ethnicity	9.01	5.96	0.14		0.13	2.01	9.13	0.03		0.83
Age	0.06	0.15	0.04		0.69	-0.36	0.20	-0.25		0.07
Pain	15.76	3.99	0.37		0.00	13.72	4.81	0.37		0.01

PO= postoperative; OR = odds ratio; CI = confidence interval; 1 = yes, 0 = no. * $p<0,05$

5 DISCUSSION

The present study demonstrated that at 6 and 12 months postoperatively, only the presence of pain was a predictor of upper limb functionality, after adjustment for clinical and sociodemographic variables. The presence of pain was associated with an increase of 15.76 (6 months PO) and 13.72 (12 months PO) units in the MS functionality score. These results indicate the need for a better follow-up monitoring for pain and functionality in the long term. Long term rehabilitation access including strategies to better control pain, as neuromodulation, should be largely available for this population.

Another study also observed that the symptom of pain negatively affects the functionality of upper limbs among breast cancer survivors [8]. This association between pain and functionality may be related to the limitations of basic activities of daily living, since pain can trigger joint limitations, alterations in movement, and muscle weakness [14], [13]. The pain in breast cancer survivors has a diffuse origin.

It was observed that the participants from the 6 month PO group presented more episodes of pain (71.4%), compared to the 12 month PO group (57.3%). Nevertheless, the intensity of pain in the trunk regions was lower in the 6 month group compared to the group of 12 month. These results may be related to the adjuvant treatments received by them. At 6 months, pain is more unavoidable and ends up being accepted as part of the patients' daily lives. Moreover, as it is the earliest postoperative period, the emotional factors may influence the physical symptoms [22], [29]. Meanwhile, at 12 months postoperative, the active phase of adjuvant treatments is almost or completely finished and, gradually, the return to daily activities is more stable and routine. In this period, the other psycho-emotional factors are being softened [22], and the physical complaints begin to gain importance due to the resumption of multiple tasks.

In both groups in this study, the regions most affected by pain were, respectively, the anterior trunk, lateral trunk and the upper limb homolateral to the surgery, similar to other previous studies [14], [23]. In the anterior trunk, pain can be related to factors linked to the surgery and to the surgical incision, which effectively provoke tissue injury [11]. Additionally, the influence of radiotherapy treatment must also be considered, which is a risk factor for developing persistent pain [4], [14]. This persistent pain behavior underlies the importance of the long-term follow-up of these patients.

Regarding pain in the lateral trunk, it is mainly due to axillary interventions that are associated with persistent pain [25]. There is evidence that axillary lymph node resection can lead to injury to nerve, muscle, and lymphatic structures in this region, which contributes to this complaint [11]. Moreover, axillary interventions can generate lymphedema, sensations of heaviness, and fatigue in the affected upper limb, which are equally uncomfortable [25]. On the other hand, at 6 months postoperatively the functional limits need to be reviewed, since the abduction movement with external rotation is commonly required during radiotherapy. Thus, it is believed that part of this pain could be minimized if there was an early and effective health education. In addition, the fact

that we did not control lymphedema and its possible relation with pain and functionality may allow exploring future analyses that are different to those addressed here.

Another region with greater involvement of pain was the upper limb homolateral to the surgery. This symptom is known [14] and may have a multifactorial cause; however, chemotherapy, for example, can cause a systemic disorder, which contributes to the onset of pain in joints and changes in muscle dynamics [26]. Radiotherapy, on the other hand, causes a decrease in tissue mobility and directly influences muscle contraction, which also affects the quality of movements [27]. We chose to include women in the active phase of treatment, since it would be the closest to the reality of Brazilian public services where problems both in diagnosis and treatment are part of the routine of this service, which negatively impacts the evolution of the clinical picture in the short and long term.

Unlike another study [7], the sociodemographic variables of our study did not behave as predictors in the functionality of the upper limbs, in both PO periods. Possibly because they are patients with older ages who often withdraw from work activities motivated by post-breast cancer health leave. In our study, the clinical characteristics of treatments also did not behave as predictors in the functionality of upper limbs in both periods of PO, which is similar to the findings of a previous study [8]. Usually, women cope with the new impacts of adjuvant treatments in the first months after surgery, and past this period they live better with the adverse consequences [8], which might explain why clinical variables were not associated to functionality at 6- and 12-months PO. Heterogeneity and complexity of treatments are dependent on individual factors of each woman and the characteristics of the cancer itself [8].

The possible limitations of the study are the Quick-Dash, which, despite being an instrument used to evaluate upper limb disability in this population, presents a certain subjectivism, since it considers the self-report in the last 7 days prior to the moment of analysis to reduce memory bias. Future studies with robust samples could differentiate groups with and without axillary lymph node resection at different postoperative times, and their relation with functionality, longitudinally.

In conclusion, women who underwent breast cancer surgery presented pain of moderate intensity, both at 6 and 12 months postoperatively, mainly in the anterior trunk region and in the upper limb homolateral to the surgery. Among the predictors analyzed

in this study, only pain influenced a decrease in functionality of the upper limbs both at 6 and 12 months postoperatively. The knowledge of this predictability by the health teams allows the adjustment of conducts in view of the present kinetic-functional alterations. Making the management of these women as safe as possible, as well as creating programs to minimize temporal mismatches in the rehabilitation process, in different socioeconomic and cultural contexts, could be an imminent alternative.

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