

Fatigue in Women with Breast Cancer Submitted to Radiotherapy

doi: <https://doi.org/10.32635/2176-9745.RBC.2019v65n2.89>

Fadiga em Mulheres com Câncer de Mama Submetidas à Radioterapia

Fatiga en Mujeres con Cáncer de Mama Sujeto a Radioterapia

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Abstract

Introduction: Fatigue in women with breast cancer after radiotherapy is one of the most debilitating side effects, being a subjective, multidimensional, multifactorial symptom. **Objective:** To characterize fatigue in patients with breast cancer in radiotherapy who undergo treatment in the radiotherapy service of a reference hospital in cancer treatment in the State of Goiás. **Method:** This is a longitudinal study. The Piper Fatigue Scale - revised was used to evaluate fatigue at the beginning (T1), middle (T2) and final (T3) of the radiotherapy. **Results:** The sample consisted of 89 women. The prevalence of T1 fatigue was 26.9%. There was a significant increase in fatigue during radiotherapy, and in T3, 50.8% of the women presented fatigue. There was a predominance of moderate fatigue in T2 and T3, and the most significant increase in fatigue intensity was verified from T1 to T2. The affective dimension of fatigue presented a higher score compared to the sensorial/psychological dimensions. **Conclusion:** The presence and intensity of fatigue during radiotherapy increased significantly, with moderate fatigue predominating in the last week of treatment. The magnitude of fatigue exhibited higher scores in the affective dimension of the evaluations. Therefore, health professionals must focus more attention to fatigue during radiotherapy.

Key words: Fatigue; Breast Neoplasms/radiotherapy; Radiotherapy/adverse effects; Longitudinal Studies; Women.

Resumo

Introdução: A fadiga em mulheres com câncer de mama após a radioterapia é um dos efeitos colaterais mais debilitantes, sendo um sintoma subjetivo, multidimensional e multifatorial. **Objetivo:** Caracterizar a fadiga em pacientes com câncer de mama em radioterapia que realizam o tratamento no Serviço de Radioterapia de um hospital de referência em tratamento oncológico do Estado de Goiás. **Método:** Trata-se de um estudo longitudinal. A Escala de Fadiga de Piper - revisada foi utilizada para avaliação de fadiga no início (T1), meio (T2) e final (T3) da radioterapia. **Resultados:** A amostra foi composta por 89 mulheres. A prevalência de fadiga em T1 foi de 26,9%. Houve aumento significativo da fadiga ao longo da radioterapia, sendo que, em T3, 50,8% das mulheres apresentavam fadiga. Houve predomínio da fadiga moderada em T2 e T3, e o aumento mais significativo da intensidade da fadiga foi verificado do momento T1 para T2. A dimensão afetiva da fadiga apresentou escore mais alto comparado às dimensões sensorial/psicológica. **Conclusão:** A presença e a intensidade da fadiga durante a radioterapia aumentaram significativamente, predominando a fadiga moderada na última semana do tratamento. A magnitude da fadiga exibiu escores mais altos na dimensão afetiva nas avaliações. Portanto, atenção maior à fadiga durante a radioterapia precisa ser dada pelos profissionais de saúde. **Palavras-chave:** Fadiga; Neoplasias da Mama/radioterapia; Radioterapia/efeitos adversos; Estudos Longitudinais; Mulheres.

Resumen

Introducción: La fatiga en mujeres con cáncer de mama después de la radioterapia es uno de los efectos colaterales más debilitantes, siendo un síntoma subjetivo, multidimensional, multifactorial. **Objetivo:** caracterizar la fatiga en pacientes con cáncer de mama en radioterapia que realizan el tratamiento en el servicio de radioterapia de un hospital de referencia en tratamiento oncológico del Estado de Goiás. **Método:** Se trata de un estudio longitudinal. La Escala de Fatiga de Piper - revisada fue utilizada para evaluación de fatiga al inicio (T1), medio (T2) y final (T3) de la radioterapia. **Resultados:** La muestra fue compuesta por 89 mujeres. La prevalencia de fatiga en T1 fue de 26,9%. Se observó un aumento significativo de la fatiga a lo largo de la radioterapia siendo que, en T3, el 50,8% de las mujeres presentaban fatiga. Se observó un predominio de la fatiga moderada en T2 y T3, y el aumento más significativo de la intensidad de la fatiga fue verificado del momento T1 para T2. La dimensión afectiva de la fatiga presentó una puntuación más alta en comparación con las dimensiones sensorial/psicológica. **Conclusión:** La presencia e intensidad de la fatiga durante la radioterapia aumentó significativamente, predominando la fatiga moderada en la última semana del tratamiento. La magnitud de la fatiga exhibió escores más altos en la dimensión afectiva en las evaluaciones. Por lo tanto, los profesionales de la salud deben prestar mayor atención a la fatiga durante la radioterapia.

Palabras clave: Fatiga; Neoplasias de la Mama/radioterapia; Radioterapia/efectos adversos; Estudios Longitudinales; Mujeres.

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INTRODUCTION

According to information from “Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA)”, breast cancer is the first cause of death by cancer in Brazil and for 2018, 59,700 new cases of breast cancer are expected¹.

Radiotherapy or teletherapy among the treatments utilized in the therapy of breast cancer is one of the most indicated to treat the disease². However, despite being effective, radiotherapy affects the quality of life and the body balance of the individual, triggering fatigue, nausea, loss of appetite, loss of hair, depression, weight gain, respiratory difficulty, sleeping disorders and loss of muscle strength³.

Fatigue in women with breast cancer after radiotherapy is one of the most debilitating side effects, it may affect 84% to 86% of the patients, being a subjective, multidimensional and multifactorial symptom⁴. Fatigued patients express feelings of tiredness, inability to keep the usual routine, loss of libido, verbalization of constant listless among others⁵.

Therefore, this symptom is more frequent in the last week of radiotherapy, because as severe the fatigue is prior to radiotherapy, more intense this symptom will be during the treatment with ionizing radiation. In addition, it is evident that, overall, fatigue returns to pre-treatment level two to three months after the end of the radiotherapy⁶.

Fatigue is a tough symptom to cope, with still not fully understood physiopathology; hence, control the evolution of the condition since the onset of the disease is primordial and is within the competence of the interdisciplinary team⁷. Because fatigue is an experience that has a significant negative repercussion⁸, it is of utmost relevance to characterize this symptom in patients submitted to radiotherapy.

In that direction, the evaluation of fatigue in breast cancer patients in conventional radiotherapeutic treatment is essential to plan individualized interventions as the organization of the cycle activity/rest, nutritional guidances and management of causal factors as depression or anemia⁸.

Based in this setting, this study is justified because it is necessary to explore the aspects of fatigue in breast cancer patients submitted to radiotherapy due to the paucity of the existing knowledge about this multidimensional experience in studies in Brazil and worldwide as well as about its characteristics, dimensions, intensity and evolution. That scenario is an obstacle for health professionals to plan more effective actions to prevent and treat the symptom. Aware of this, the present study was elaborated, attempting to characterize fatigue of women with breast cancer submitted to conventional radiotherapy

and the presence, intensity and magnitude of the sensorial/psychological, affective and behavioral dimensions based in the Piper Fatigue Scale^{9,10}.

METHOD

Prospective cohort study with follow up in three moments. The sample consisted of 89 women with diagnosis of breast cancer in conventional radiotherapy treatment. Data collection was performed at the Radiotherapy Service of an oncological reference hospital of the State of Goiás in compliance with Resolution 466/12 of the National Health Council. The Institutional Review Board of the hospital reviewed and approved the project to which this study is part, Report number 544.604, CAAE:14552713.3.0000.0031.

The inclusion criteria were: females, breast cancer in any staging, 18 years old or older, indication of 20 or more fractions of radiotherapy with minimum dose of 180 cGy/day, preserved ability to communicate and understand. The exclusion criteria were: concomitant chemotherapy and radiotherapy, suspension of radiotherapy for 15 days or more or three or more suspensions, regardless of the number of days.

The study participants were enrolled between July 2015 and April 2016 during visits with trained nurses and undergraduate nursing students. These visits were conducted during three days of the week in the hospital's radiotherapy service and those who met the inclusion criteria were invited to join the study. After reading, clarification of doubts and signature of the informed consent form in two copies, the participants were interviewed while waiting for the radiotherapy session in a secluded office for data collection. Therefore, the study information were formed by data obtained from the interview in three moments: the first moment, since the simulation until the fourth or fifth session of radiotherapy (T1); the second, 15 days after the beginning of radiotherapy \pm two days (T2); and the third, in the last week of the treatment (T3).

Piper Fatigue Scale revised validated for use in Brazil in 2009 was utilized to assess fatigue¹⁰. It is a self-report multidimensional instrument consisting of 22 closed items and four open items. The 22 items address three dimensions of fatigue: behavioral, affective, sensorial-psychological. Each item is presented in a numerical scale (0 to 10) and the total score is calculated by the mean of all the items of the instrument and the scores of the dimensions are calculated from the mean of the items contained in each dimension, the highest scores indicate more fatigue^{9,10}. The patients were considered fatigued when their scores were different from zero in the Piper

Fatigue Scale – revised, according to the suggestion of the consensus *National Comprehensive Cancer Network* for classification of fatigue that defined the cut-off in score 4 to distinguish fatigued from non-fatigued individuals. In addition, to classify the intensity of the fatigue based in the total score, three levels were defined: mild (score higher than 0 and lower than 4); moderate (score equal or higher than 4 and lower than 6) and severe (score equal or higher than 6 until 10)¹¹.

Further to data collection about fatigue, it included cancer-related sociodemographic, clinical data, and respective treatment through an instrument developed by the investigators involved in the clinical trial. These data characterized the sample in study.

The information obtained were tabulated in a Microsoft Excel® spreadsheet and the results presented as spreadsheets, charts and/or tables described in absolute figures and percentage. It was utilized the *Statistical Package for Social Science* (SPSS) to analyze the data and it was considered a level of significance of 5% for all the tests. The scores obtained in the Piper Fatigue Scale revised presented normal distribution in the three moments (T1, T2 and T3). Parametric tests evaluated the difference between the means of the dimensions of fatigue and the total score of fatigue in a same moment of evaluation (test t for one sample) and the analysis of variance (Anova) for repeated measures to assess the difference between the means of a same domain and the total score during the three moments of evaluation.

RESULTS

During the period of the study, 89 women were enrolled in the cohort (T1); of these, 86 patients were evaluated in T2 and 81 in T3 with eight losses during the three evaluations, among them, one loss because the patient refused to participate of the subsequent evaluations, another, due to suspension for more than 15 days and four, because of impossibility to be interviewed at the proper time by the investigators. It were excluded of the study the patients that started chemotherapy concomitant to radiotherapy during the evaluations.

Overall, the study patients received fractioned doses of radiotherapy that varied from 180 to 267 cGy and all of them were submitted to surgery prior to radiotherapy. In addition, according to the staging of the tumors pursuant to the classification of malignant tumors, 43 (48.3%) women were in stage III, 37 (41.6%) in stage II and nine (10.1%) in stage I¹².

As presented in Table 1, the sample consisted of 89 patients, mean age of 53.9 years; until six years of education (53.4%); predominance of per capita income

Table 1. Distribution of women submitted to radiotherapy according to the clinical and sociodemographic characteristics. Goiânia, GO, Brazil, 2015 (n=89)

Characteristics		
Age:	53.9 years (14.9);	
Mean (SD); min.-max.	31.0-83.0	
	n	%
Education (years)		
0-7	47	53.4
7-20	41	46.6
Per capita income		
<1 MW	59	67.8
2-4 MW	28	32.2
With spouse		
Yes	53	60.2
No	35	39.8
Color of Skin		
Caucasian	34	38.6
Brown	42	47.7
Black	7	8.0
Asian	5	5.7
Indian	0	0.0
Tobacco		
Smoker	82	92.1
Non smoker	07	7.9
Neoadjuvant chemotherapy		
Yes	35	39.3
No	54	60.7
Adjuvant Chemotherapy		
Yes	44	49.4
No	45	50.6
BMI (Kg/m²)		
≤25	37	41.6
>25	52	58.4
Hormone therapy		
Yes	30	34.5
No	57	65.5
Hemoglobin (g/dl)		
≥8 and <10	2	3.2
≥10 and ≤12.4	36	58.1
>12.5	24	38.7
Interruption of the treatment		
Did not interrupt	57	65.5
Interrupted	30	34.5
Comorbidity		
Presence of ≥1	75	84.3
Absence	14	15.7

Captions: MW = Minimum wage; SD = Standard Deviation; BMI = Body Mass Index.

lower than one minimum wage (6788%); the majority of the patients (60.2%) had a stable spouse and did not smoke (92.1%).

Neoadjuvant chemotherapy was administered in 39.3% of the patients and adjuvant chemotherapy in 49.4% of the sample. Still, 61.3% of the patients presented hemoglobin ≤ 12.4 g/dl. The interruption of the treatment was noticed in 30 women (34.5%). Of these, 20 (66.6%) interrupted for three or less than three days, six (20.0%) interrupted for four to eight days and the other four (13.3%) interrupted for nine to 14 days. The motive for these interruptions were related to transportation to the hospital as reported by the patients, temporary suspension of the activity of the radiotherapy instruments due to malfunction and servicing and skin complications (radiodermatitis) resulting from radiotherapy (Table 1).

According to Table 2, the prevalence of fatigue in the beginning of the treatment was present in 26.9% of the patients and new cases of fatigue were identified along radiotherapy. In relation to the intensity of fatigue in T1 there is an equal number of women with mild and moderate fatigue. In T2 and T3, it was identified predominance of moderate fatigue among the study patients, with 20.9% and 32.1% respectively. Overall, based in the total score, a greater number of women, 32.1% had moderate level of fatigue at the end of the treatment with mean score of 6.0% (SD = 1.7).

The mean intensity of fatigue for each dimension of the Piper Fatigue Scale and in every moment of the study is presented in Table 3. It was evidenced a gradual increase of the mean intensity in the three moments of the study (T1, T2 and T3), either for the total score or for each dimension. The Anova test for repeated measures was carried out to evaluate the null hypothesis that there were no change in the scores of total fatigue and by dimension during the radiotherapy. The results indicate significant effect throughout the therapy (Wilks Lambda=0,821, $p < 0,001$). Therefore, there is evidence to reject the null hypothesis. Comparisons pairwise indicated that the difference was significant ($p = 0.001$ and $p < 0.001$, respectively) between total fatigue in T1 and T2, in T1 and T3. The difference between the scores of the behavioral dimension of fatigue was significant between T1 and T2 ($p = 0.015$) and between T1 and T3 ($p = 0.001$). The difference between the scores of the affective dimension of fatigue were significant between T1 and T2 ($p = 0.003$) and between T1 and T3 ($p < 0.001$). Significant differences were also observed between the scores of sensorial/psychological dimension between T1 and T2 ($p = 0.003$), between T1 and T3 ($p < 0.001$) and between T2 and T3 ($p < 0.001$).

Table 2. Classification of fatigue according to the original categories of the Piper Fatigue Scale in the 1st evaluation (T1), 2nd evaluation (T2) and 3rd evaluation (T3). Goiânia, GO, Brazil, 2015 (n=89)

	Presence of Fatigue	Classification of fatigue n (%)		
	n (%)	Mild	Moderate	Severe
T1(n=89)	24 (26.9)	10 (11.2)	10 (11.2)	4 (4.5)
T2(n=86)	35 (40.7)	5 (5.8)	18 (20.9)	12 (14.0)
T3(n=81)	41 (50.6)	3 (3.7)	26 (32.1)	12 (14.8)

Table 3. Classification of fatigue according to continuous intensity and dimensions of the Piper Scale in the 1st evaluation (T1), 2nd evaluation (T2) and 3rd evaluation (T3). Goiânia, GO, Brazil, 2015 (n=89)

	Mean intensity of fatigue (standard deviation)		
	Behavioral†	Affective†	Sensorial/Psychological†
T1*	5.0 (2.2)	6.9 (2.4)	5.1 (2.6)
T2*	5.7 (2.2)	7.5 (2.5)	5.6 (2.0)
T3*	6.1 (2.0)	8.2 (2.3)	5.7 (1.9)
Total	5.2 (2.1)	6.0 (1.9)	6.4 (1.8)

Captions: *Test Anova performed at each moment of the evaluation T1, T2 and T3; †Test t performed in each dimension.

Concerning the magnitude of this symptom in the dimensions evaluated by the scale, the means of the scores of affective dimension of fatigue were significantly bigger ($p = 0.02$) than the mean of the scores of each one of the behavioral, sensorial/psychological dimensions and of the total score in T1, T2 and T3 (Table 3). In T3, there was also significant difference between the score of the sensorial/psychological dimension and the total score of fatigue. There was no significant difference among the other dimensions of the Piper Fatigue Scale and the total score.

Among the women that reported fatigue, part responded to the Piper open questions: in T1, 10 of 24, in T2, 22 of 35 and in T3, 15 of 41 responded. The fatigued patients in T1 reported they experienced fatigue for seven months (SD = 3.8; median = 7), in average.

According to the fatigued participants in T1, chemotherapy was considered the most common cause of fatigue followed by emotional factors (stress, fear, uneasiness) and the cancer itself. In T2, chemotherapy was mentioned as cause of fatigue, but radiotherapy was the cause most commonly referred, followed by cancer, radiotherapy-related problems (daily locomotion, duration of the treatment, waiting time, hospital environment, temporary accommodations, for example),

personal problems (unemployment, financial problems, sons, etc.) and emotional factors (stress, concern, anxiety). In T3, all the interviewee reported radiotherapy as being one of the causes of fatigue. In addition, it were also referred the previous chemotherapy treatment and emotional and personal factors mentioned formerly.

Activities of leisure as stroll, socialize with family and friends, watch television, mobile or computer games were reported as the preferred by the fatigued participants in T1 for relief of fatigue, followed by rest and sleep. One woman mentioned religious and physical activities. In T2, the most mentioned action to relieve fatigue was rest and sleep; other actions mentioned in lower number were leisure, physical, religious activities and work. Similar to moment T2, in T3 the majority of women reported rest and sleep as the most preferred actions to relieve fatigue. In addition to the other leisure, physical and religious activities less mentioned, there was one case who reported alternative therapies (herbs).

For all three evaluations, somnolence was the most common mentioned to characterize the sensation of fatigue. When questioned about the presence of other symptoms in T1, the symptoms mentioned were pain (n=40, 44.9%) and sleeping disorders (n=21, 23.6%). In T2, pain was referred by 38 (44.2%) and sleeping disorders by 28 (32.6%) women. In T3, the report of pain and sleeping disorders was 39 (48.1%) and 31 (38.3%), respectively.

DISCUSSION

This study evaluated the fatigue in three moments since the simulation of radiotherapy until the fourth or fifth session of radiotherapy (T1), four weeks after the beginning of the radiotherapy \pm two days (T2) and in the last week of the treatment (T3). While describing the detailed data about the evolution of the fatigue during the radiotherapy treatment, the present study brings data that contribute with solid evidences on fatigue in women with breast cancer submitted to conventional radiotherapy.

The cancer-related studies about fatigue indicate it is a common and treatable symptom that interferes significantly in several aspects of the life of the patients with breast cancer and is related to multiple factors including the radiotherapy treatment. Consequently, patients report fatigue as one of the most important and stressing cancer-related symptoms and its treatment¹³⁻¹⁵. Nevertheless, despite the increase of the levels of fatigue resulting from cancer treatment whereas is not yet a consensus in the literature, because of its multidimensional and multifactorial character, studies report the expansion of the presence and intensity of this symptom along the

radiotherapy, being an independent factor able to interfere in the quality of life and in the cognitive-behavioral aspects^{13,15-18}.

In the present study, fatigue was present in 24 patients (26.9%) since the beginning of radiotherapy (T1), even in women that have not initiated radiotherapy, and in the third evaluation, more than half of the women presented this symptom (50.8%). This is object of concern as much as the pre-treatment level of fatigue may be an important risk factor for chronic fatigue and decline of the quality of life as encountered in a study conducted in Germany where it was evaluated the pre and post-radiotherapy levels of fatigue¹⁹.

In investigations that utilized the same cut-off (≥ 4) for the evaluation of this symptom, it was observed the variation of the presence of fatigue. In a study conducted in the city of São Paulo, 31.9% of the sample of 163 patients with breast cancer presented fatigue clinically relevant²⁰.

Having in mind that many patients of this study initiated the treatment with some degree of fatigue, based in the classification of intensity of fatigue (mild, moderate, severe), in the last moment of the evaluation, nearly half (47%) presented moderate and severe fatigue (Table 2); in the study of Lamino et al.²⁰, the authors found predominance of moderate and severe fatigue in 64.2% of the patients.

In another study conducted in Greece with 106 patients with breast cancer in radiotherapy 13% of the patients presented moderate to severe degree of fatigue in the beginning of the radiotherapy¹⁵. Therefore, said results indicate the importance to identify these patients in initial staging to allow that proper investigations are implemented.

The mean intensity of fatigue in the end of the radiotherapy in the study women was 6.0 (SD=1.7), which indicates moderate fatigue (Table 3). In addition, the most significant increase of the presence of fatigue ($p < 0.05$) as verified from the moment T1 to T2 with raises of 86.6% and 211.1% respectively (Table 2).

In relation to the magnitude of this symptom, the affective symptom predominated when compared to the other dimensions evaluated. Knowing that this dimension attempts to identify the meaning or the interpretation attributed to fatigue, this result indicates to what extent it can interfere negatively in the life of the patients because of its destructive, unacceptable and unpleasant character¹⁰. Consequently, the professionals must include interventions that involve the affective dimension of the individual, developing the self-efficacy of the women and showing that fatigue is a symptom that can be controlled, even if not cured.

Considering the reality experienced in the site data were collected and while exchanging experiences with peers from other radiotherapy services in Brazil, it is notorious the necessity to capacitate the professionals for diagnosis and management of fatigue. In the present study, it is possible to presume that this symptom has escalated since the beginning of radiotherapy without intervention by the professionals for its reduction and relief, it is important to highlight that fatigue can restrain or obstruct the continuity of the treatment^{16,17,20-22}. Still more serious, based in the actions followed by women to relief fatigue, the majority decided to rest or sleep, which is less recommended to control fatigue.

At last, it is recognized that fatigue is one of the problems of the woman with breast cancer in radiotherapy. Other symptoms commonly reported, pain and sleeping disorders, may onset in cluster of symptoms and affect the intensity of the fatigue. Consequently, health caregivers must be proactive in prevention, identification and control of the human responses to cancer and its treatment adopted.

The current investigation contributes to expand the understanding about fatigue and radiotherapy as independent factor of cause of this symptom. Therefore, oncologic treatment in women with breast cancer demands extreme capacity of adaptation to the new conditions unfolding from this process. Moreover, despite the limited assistance to fatigue, women recognize by their own that radiotherapy is the important cause of the symptom. In face of this, these results are object of concern because it is a symptom characterized as clinically relevant in the patients with breast cancer, specially these women that had severe fatigue in the end of the treatment^{12,17,20,22}.

CONCLUSION

The presence and intensity of the fatigue during radiotherapy increased significantly, predominating moderate fatigue in the last week of the treatment. Furthermore, with the characterization of the fatigue in relation to the magnitude, by the dimensions of the Piper Fatigue Scale revised it was identified that the affective dimension prevailed with higher scores for all the evaluations showing the negative perception of the patients with this symptom, being referred as destructive, abnormal and unpleasant in their lives.

These results contribute to the raising body of evidences about radiation-induced fatigue and provide an important base for effective and appropriate interventions by the nursing and multiprofessional team involved in caring for these women. Consequently, this study reflects the

necessity of health professionals to focus more attention to fatigue during radiotherapy, using proper scales for early detection and relief of this symptom that provokes suffering and harm to the quality of life of the patients.

CONTRIBUTIONS

All the authors contributed substantially for the conception and planning of the study, gathering, analyzing and/or interpretation of data, as well as wording and critical review of the final approval of the version published.

DECLARATION OF CONFLICT OF INTERESTS

There are no conflict of interests to declare.

FUNDING SOURCES

None.

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Recebido em 10/3/2019
Aprovado em 9/10/2019