

Impact of fatigue on the quality of life of women with breast cancer
Impacto da fadiga na qualidade de vida de mulheres com câncer de mama
Impacto de la fatiga en la calidad de vida de las mujeres con cáncer de mama

Received: 13/11/2019

Approved: 07/06/2020

Published: 01/07/2020

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This study aimed to evaluate the quality of life of women with fatigue caused by chemotherapy during breast cancer treatment. This is a prospective and quantitative study with 47 women cared by a university hospital. We collected data between 2017 and 2018 at two stages (T1 and T2) with specific tools to measure fatigue and quality of life. Most women had moderate fatigue, in which the affection dimension was the most affected, and their quality of life was reasonable. The correlation between total fatigue and general health, social function and pain were significant only at T2; which suggests that the more persistent the fatigue, the greater the compromise to quality of life can be. The study showed that fatigue compromises women emotionally and socially. It is necessary to investigate more effective measures for the management of fatigue and restoration of quality of life.

Descriptors: Fatigue; Drug therapy; Quality of life; Breast neoplasms; Women.

O objetivo deste estudo foi avaliar a qualidade de vida de mulheres com fadiga secundária à quimioterapia durante o tratamento para o câncer de mama. Trata-se de um estudo prospectivo, quantitativo, com 47 mulheres atendidas em um hospital universitário. Os dados foram coletados entre 2017 a 2018 em dois momentos (T1 e T2), através de instrumentos de mensuração específicos para fadiga e qualidade de vida. Houve predomínio de mulheres com fadiga moderada, a dimensão afetiva foi a mais afetada, e a qualidade de vida apresentada foi razoável. As correlações entre fadiga total e estado geral de saúde, função social e dor foram significativas apenas em T2; o que sugere que quanto mais persistente a fadiga, maior poderá ser o comprometimento da qualidade de vida. O estudo mostrou que a fadiga compromete funcional, emocional e socialmente as mulheres; sendo necessário investigar medidas mais efetivas para o gerenciamento da fadiga e para o restabelecimento da qualidade de vida.

Descritores: Fadiga; Tratamento farmacológico; Qualidade de vida; Neoplasias da mama; Mulheres.

El objetivo de este estudio fue evaluar la calidad de vida de las mujeres con fatiga secundaria a la quimioterapia durante el tratamiento del cáncer de mama. Es un estudio prospectivo y cuantitativo con 47 mujeres atendidas en un hospital universitario. Los datos se recopilaron entre 2017 y 2018 en dos momentos (T1 y T2), utilizando instrumentos de medición específicos para la fatiga y la calidad de vida. Predominaban las mujeres con fatiga moderada, la dimensión afectiva fue la más afectada y la calidad de vida presentada fue razonable. Las correlaciones entre la fatiga total y el estado general de salud, la función social y el dolor fueron significativas sólo en T2; lo que sugiere que cuanto más persistente sea la fatiga, mayor puede ser el deterioro de la calidad de vida. El estudio demostró que la fatiga compromete a las mujeres funcional, emocional y socialmente; y es necesario investigar medidas más eficaces para el manejo de la fatiga y el restablecimiento de la calidad de vida.

Descritores: Fatiga; Quimioterapia; Calidad de vida; Neoplasias de la mama; Mujeres.

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INTRODUCTION

Breast cancer is considered a complex illness that demands painful treatments and generates uncertainty about its cure, which impacts the lives of women from the moment they receive the diagnosis all the way to treatment and rehabilitation¹.

In regards of treatments, chemotherapy (CT) represents the course of treatment taken in most cases. This treatment consists on the ministrations of drugs that halt or diminish the growth of cancerous cells; and it happens in cycles that may be daily, weekly or monthly, and that are intersected with periods of rest. During CH, healthy cells are also affected, which usually causes adverse side effects².

Fatigue is a symptom directly linked to cancer itself and to side effects of treatments such as CH. It is reported as asthenia, lethargy, exhaustion; a feeling of weakness, extreme tiredness, a lack of motivation, among others³.

Fatigue due to chemotherapy (FDC) can interfere with everyday activities and it has a considerable repercussion on social well-being, therefore damaging social and professional activities, as well as the interpersonal relationships of the sick individual. Because of this, FDC is a strong predictor to a decrease in Quality of Life (QL)⁴.

Many health professionals do not evaluate FDC because they do not know or do not realize its effects on QL, and also because there is a lack of studies that evaluate fatigue during, and exclusively on, CT to support the practice. So, studies such as this are important, because they confirm the occurrence of fatigue, and they provide assistance so professionals can develop suitable interventions for prevention, management and control of this particular side effect, in order to guarantee positive results on the course of treatment and, consequently, maintain or improve the patients' QL. This study aimed to evaluate the QL of women with fatigue due to chemotherapy during treatment of breast cancer.

METHOD

This is a prospective, quantitative study. It was carried out at the oncology outpatient clinic of a university hospital, from May of 2017 to March of 2018. In this particular clinic, we invited women with breast cancer who underwent CT to participate in an Extension Project (EP) that offered guidance through appointments with nurses about the prevention of undesirable side effects and management of adverse reactions.

During the appointments held at the EP, any patient who presented complaints about fatigue, and whose complaints fit into any of the defining characteristics for the diagnosis of fatigue, was approached and invited to participate in the research⁵.

The sample was composed by women who met the following inclusion criteria: women diagnosed with breast cancer, without distant metastasis, over 18 years of age, currently undergoing chemotherapy, with FDC, with no history of prior fatigue, with preserved cognitive ability, participating on the EP and who formally expressed an interest in participating in the research by signing the Free and Informed Consent Form (ICF).

Women who gave up on participating after having already started, who had their treatment regimen changed after the beginning of the study, who had distant metastases during the treatment, and who missed the follow-up due to reasons such as hospitalization were excluded.

We collected the data during two distinct moments: when FDC was first identified (T1), and on the subsequent chemotherapy cycle (T2). In order to characterize the investigated population, we took data from their medical files and on their socio-demographic characterization forms. Also, for the evaluation of FDC, we used the Fatigue Pictogram (T1) and Revised Piper Fatigue Scale (T1 and T2)^{6,7}. To evaluate the QL, we applied the *European Organization for Research and Treatment of Cancer 30-Item Quality of Life Questionnaire* (EORTC QLQ-C30), version 3.0, in Portuguese, in T1 and T2⁸.

We calculated the total score of the Revised Piper Fatigue Scale through the average of the items, while we used the average of the items contained in each dimension to calculate the scores of the dimensions. For this study, we used the following classification: absence of fatigue - score 0; mild fatigue - score $0 < 4$; moderate fatigue - score $4 \leq 6$; intense fatigue - $6 \geq 10$.

To calculate EORTC QLQ-C30 scores, we used the Scoring Manual¹⁰. Scores range from 0 to 100, and the closer to 0 the score is on the functional scale, the higher the healthy functional level; a score close to 100 on the symptom scale represents a high level of symptoms and side effects¹⁰. For comparison of results, differences in EORTC QLQ-C30 scores from 5 to 10 correspond to small changes, from 10 to 20 correspond to moderate changes, and greater than 20 are large changes¹¹.

We entered the collected data into spreadsheets in the Microsoft Excel 2016 program, with double entry for greater reliability in data transcription. Statistical analysis was performed with the help of the SPSS Windows Statistical Package for the Social Science (SPSS) software, version 22.0, for Windows. Quantitative variables were expressed by measures of central tendency and variability/dispersion.

The paired T test was used to compare the means of the variables between the two moments; and Spearman's correlation coefficient was used to analyze the correlation between variables. The level of significance was set at $p < 0.05$.

The study was approved by the Human Research Ethics Committee of the Universidade Federal de Uberlândia, under no. 1,974,478. All participants were asked to sign a Free and Clarified Consent Form, as it is required by Resolution 466/12 of the National Health Council. Anonymity of all participants was maintained through the use of pseudonyms.

RESULTS

In this study, 47 women participated. Most of women were in the 50-69 years age group (55%), white (61%), married (44%), had incomplete elementary education (53%), were employed in the services sector as sellers in stores and markets (78%), who considered themselves Catholic (38%).

Approximately 80% of women with FDC had their menarche after the age of 12, and 68% had more than one child. All women participating in this study were diagnosed with invasive breast carcinoma.

Prevalence of fatigue due to chemotherapy

With the help of the Fatigue Pictogram - which allows assessing the intensity and impact of fatigue - in the first interview (T1), 38% of women said they were "moderately tired", 36% were "a little tired", 13% were "very tired" and 11% were "extremely tired". In regards of their performances of everyday activities and the impact of FDC, 30% said that "they could do almost everything they usually did", 26% said that "they only did what they really had to do", 23% "were able to do some things", 13% "did everything they usually did", and 9% said "they managed to do very little".

Through the application of the Revised Piper Fatigue Scale, most women said they had moderate fatigue (48% in T1 and 53% in T2), followed those with intense fatigue (44% in T1 and 34% in T2); however, there was an increase in women with mild fatigue (6% in T1 and 12% in T2) and moderate fatigue - in a comparison between T1 and T2 - and a decrease in women with intense fatigue.

Table 1 shows the measures of central tendency, variability and univariate analysis of the items on the Revised Piper Fatigue Scale.

At T1, women experienced fatigue, on average, for 49 days, and at T2, for 71 days ($p = 0.00$). The difference between the average total fatigue scores was not statistically significant ($p = 0.13$). The most affected dimension was the affection dimension, followed by the sensory/psychological and behavioral dimensions; and the only dimension that showed a

statistically significant difference ($p = 0.04$), from T1 to T2, was the sensory/psychological dimension.

Table 1. Measures of central tendency, variability and univariate analysis of the items on the Revised Piper Fatigue Scale. Uberlândia, Minas Gerais, Brazil, 2018.

	Minimum		Maximum		Mean		Median		Standard deviation		p^*
	T1	T2	T1	T2	T1	T2	T1	T2	T1	T2	
Days with fatigue	18.00	35.00	151.00	179.00	49.04	71.64	42.00	62.00	35.98	34.89	0.00
Total fatigue	3.05	2.14	9.50	9.45	5.90	5.61	5.82	5.32	1.46	1.52	0.13
Behavioral dimension	1.17	0.00	9.50	9.67	5.16	5.28	4.67	5.67	2.26	2.40	0.95
Affection dimension	2.80	0.00	10.00	10.00	7.10	6.75	7.20	6.80	1.90	2.31	0.30
Psychological/sensory dimension	3.27	0.00	9.45	9.27	5.75	5.33	5.27	5.09	1.49	1.72	0.04

*T Test paired

Quality of Life

Table 2 shows the measures of central tendency, variability and univariate analysis of each scale and item in the EORTC QLQ-C30.

The study participants had a reasonable QL, but there was no significant change ($p = 0.84$) in QL between moments.

Among the functional scales, the emotional and social functions had lower averages, thus demonstrating a greater impairment of QL in these aspects.

The social function had the lowest average. This finding reveals how much FDC has influenced the QL of women with breast cancer in terms of their social and family life, and in the relationships that are established on them.

In the symptom scales, only fatigue increased at T2. However, the only symptom that presented moderate alteration was insomnia, which was not significant ($p = 0.06$).

Fatigue and financial difficulties were directly correlated ($sr = 0.23$ in T1 and $sr = 0.23$ in T2), but not significantly ($p = 0.11$ in T1 and $p = 0.11$ in T2). Even so, considering that FDC is one of the causes of absence from work during treatment, the women in this study indicated a certain financial difficulty related to treatment. The univariate analysis of the items in the EORTC QLQ-C30 did not indicate a statistically significant difference between the means from T1 to T2.

Correlation between variables

Table 3 shows the correlation between the variables of greatest interest, the Piper Fatigue Scale and the EORTC-QLQ C30. The correlations between total fatigue and general health/QL ($p = 0.01$; $sr = -0.36$), social function ($p = 0.02$; $rs = -0.33$) and pain ($p < 0, 01$; $rs = 0.48$) were significant only in T2. With this in mind, it is possible to infer that the more intense the fatigue, the worse the QL, social function and pain.

Fatigue and physical and emotional functions showed an inverse and significant correlation in the two assessed moments (T1 and T2); in T2, this correlation was strongly significant ($p < 0.01$). Thus, the more intense the fatigue, the greater the functional and emotional impairment.

These results, with a greater significance of the correlations in T2, suggest that the more persistent the FDC, the greater the QL impairment may be.

Table 2. Central tendency measures, variability and univariate analysis of EORTC QLQ-C30 scales and items. Uberlândia, Minas Gerais, Brazil, 2018.

	Minimum		Maximum		Mean		Median		Standard deviation		<i>p</i> *
	T1	T2	T1	T2	T1	T2	T1	T2	T1	T2	
General Health State/QL Functional scales	25.00	0.00	100.00	100.00	68.09	67.38	66.67	75.00	18.33	23.37	0.84
Physical function	33.33	26.67	100.00	100.00	73.48	71.63	80.00	73.33	21.10	20.92	0.53
Performance of roles	0.00	0.00	100.00	100.00	73.40	73.76	83.33	83.33	32.54	29.64	0.93
Emotional function	0.00	8.33	100.00	100.00	60.64	67.02	66.67	66.67	28.69	27.31	0.09
Cognitive function	33.33	0.00	100.00	100.00	81.91	80.85	83.33	100.00	20.80	27.14	0.70
Social function	0.00	0.00	100.00	100.00	59.22	60.99	66.67	66.67	28.19	31.33	0.69
Symptoms scale/items											
Fatigue	0.00	0.00	100.00	100.00	37.35	39.95	33,33	33.33	21.79	39.95	0.43
Nausea and Vomiting	0.00	0.00	83.33	100.00	12.41	14.54	0,00	0.00	19.80	23.47	0.53
Pain	0.00	0.00	100.00	100.00	32.27	29.43	33,33	16.67	29.98	30.14	0.51
Dyspnoea	0.00	0.00	100.00	100.00	9.93	11.35	0,00	0.00	24.98	28.04	0.66
Insomnia	0.00	0.00	100.00	100.00	34.75	23.40	0,00	0.00	41.09	33.27	0.06
Loss of appetite	0.00	0.00	100.00	100.00	34.75	31.91	33,33	33.33	36.75	33.30	0.52
Constipation	0.00	0.00	100.00	100.00	17.02	23.40	0,00	0.00	24.94	29.42	0.19
Diarrhoea	0.00	0.00	100.00	100.00	4.96	9.22	0,00	0.00	16.99	24.77	0.32
Financial difficulties	0.00	0.00	100.00	100.00	36.17	34.75	0,00	33.33	42.18	39.90	0.75

* T Test paired

Table 3. Correlation between variables of the Revised Piper Fatigue Scale and the EORTC-QLQ C30. Uberlândia, Minas Gerais, Brazil, 2018.

	T1		T2	
	<i>sr</i> *	<i>p</i> **	<i>sp</i> *	<i>p</i> **
Total fatigue and QL	-0.23	0.10	-0.36	0.01
Fatigue and physical function	-0.31	0.03	-0.38	0.00
Fatigue and emotional function	-0.35	0.01	-0.46	0.00
Fatigue and social function	-0.13	0.35	-0.33	0.02
Fatigue and pain	0.08	0.58	0.48	0.00
Fatigue and financial difficulties	0.23	0.11	0.23	0.11

*Coefficient of Spearman Correlation

**Significance

DISCUSSION

The demographic characterization of the participants in this study is similar to other studies^{12,13}.

Age of the first menstruation under 12 years and nulliparity are factors involved in the etiology of breast cancer¹⁴. Most participants had their menarche after 12 years of age and more than 2 children, but these factors did not prevent breast cancer from happening.

The findings on the impact and intensity of FDC at T1, using the Fatigue Pictogram, confirm the results of another study, in which patients with fatigue reported significant

impairment in their ability to complete a variety of activities of their daily lives, including cooking, cleaning and performing social activities with friends and family¹⁵.

A moderate fatigue score (approximately 6) was observed in the women surveyed, as well as in other studies of the same nature^{16,17}.

There was a small, but not significant, decrease in the mean FDC score from T1 to T2, which may be due to a decrease in women with severe fatigue and an increase in women with mild and moderate fatigue in T2. Contradicting the research, there was an increase in fatigue from cycle 1 to cycle 4; this difference can be explained by the longer assessment interval and the adoption of different tools for measuring the phenomenon¹⁸. In a study that evaluated pain in women with breast cancer, there was a higher prevalence of women with moderate fatigue, as our study showed¹⁹.

Among the evaluated dimensions, the affection dimension was the most affected. A woman with breast cancer, who experiences FDC deals with many feelings that were not present in her life, such as insecurity, uncertainty, fear, among others. FDC has such a profound emotional effect on patients that, in one study, about 90% of cases report a loss of emotional control, 74% of feelings of isolation and helplessness and 72% of feelings of prostration²⁰.

The behavioral dimension was also affected, with moderate results. In a study that analyzes professional and domestic performance in patients with breast cancer in CT, presence of fatigue was statistically significant in patients on leave from work, or indicates a magnitude of the functional impairment that FDC can cause²¹.

The participants in this study showed a statistically significant worsening of the sensory/psychological from T1 to T2. In a study that evaluated cognitive functioning of women with breast cancer, considerable psychological vulnerability was noticed, with high impairment in attention, memory, processing speed and executive functioning; which can interfere with the person's ability to fully participate in work, family and social activities²²⁻²⁴.

The general state of health/QL was satisfactory and similar to the result found in another study, carried out with women with breast cancer going through CT in Aracaju, in the state of Sergipe, whose score was 68.4825. When compared to the score of another study that assessed fatigue and QL in cancer patients on CT, the score on the study in question was lower¹⁷.

The participants had generally satisfactory scores on the functional scales, but were still affected by fatigue, pain, insomnia, loss of appetite and financial difficulties.

In another study, the scores were high in the aspects Physical Function, Performance of Roles, Cognitive Function, Social Function and lower in Emotional Function²⁶. This study differs only with respect to Social Function.

Fatigue and physical function showed an inverse and significant association; thus, the greater the fatigue, the worse the functional performance. In some cases, FDC is the most significant barrier for maintenance and functional recovery of patients whose disease progression is stable during CT²⁰.

The social function was the one with the lowest score, and the inverse association with fatigue, with significance at T2. In a study that assessed whether the Self-Regulation Model contributed to the understanding of FDC, fatigue had far-reaching social consequences for participants, who reported interruption in social life due to fatigue - thus generating a feeling of isolation - in addition to the difficulty of coping with social pressure to return to normal; which results in a significant decrease in general QL²⁷.

Fatigue and emotional function showed an inverse and significant association. Breast cancer can trigger several negative feelings in women, and these may be strongly related to changes in their QL. Among these feelings, we can highlight the fear of the diagnosis, of possible surgery, the uncertainty of the prognosis and the recurrence of the side effects of treatment, pain and facing the possibility of death²⁸.

Pain presented one of the highest scores, with a strongly significant correlation between pain and fatigue in T2, representing an impact on QL. In a study previously carried out, a

positive, moderate and statistically significant correlation was noticed between pain and fatigue and that these occur concomitantly, one worsening the other¹⁹.

Insomnia decreased moderately, but not significantly, at T2. Women undergoing chemotherapy for breast cancer often have difficulty sleeping and bad sleep quality, which may be related to behavioral, social and physiological factors, stemming from their experience with the disease and concerns about their future health²⁵⁻²⁹.

Loss of appetite was one of the symptoms that had the highest score, behind fatigue and insomnia. Loss of appetite can have an impact on women's QL, which can cause nutritional problems that negatively reflect on their physical state and self-image, and it is necessary to provide guidance and take measures to overcome the loss of appetite felt by women²⁵.

Although the correlation between fatigue and financial difficulties was not significant, the women in this study indicated a certain financial loss in relation to treatment, as well as in another investigation²⁵. The economic impact is not limited to the patients themselves, but also extends to caregivers and family members, many of whom worked less hours to provide care for the sick person²⁰.

FDC has somehow impacted women with breast cancer and their QL, especially in regards to social function and emotional/affective function.

CONCLUSION

The participants in this study showed a predominance of moderate fatigue during CT, with greater affection impairment. The findings indicate that FDC promotes changes in QL, and compromises women functionally, socially and emotionally; and still suggest that time can be an important predictor for worsening QL; the longer a woman lives with fatigue, the more compromised her QL may be.

The limitations of this study are related to the non-probabilistic sample, which prevents generalizations; and the number of assessments and the interval between them, which may have been reduced to allow better visualization of the effect of FDC over time, in turn brings contributions considering the scarcity of studies relating QL in women with breast cancer and fatigue during, and exclusively in chemotherapy treatment.

In light of this, the importance of the multidisciplinary team's performance in seeking appropriate forms of identification, management and treatment of fatigue, working with the patients and their caregivers, is highlighted, in addition to the development of more studies with this group - with more evaluations throughout the year. treatment - that aim to establish more accurately the pattern of occurrence of FDC and its effect over time.

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CONTRIBUTIONS

Anna Cláudia Yokoyama dos Anjos, Cristiane Soares Campos, Maria Beatriz Guimarães Ferreira and Taliana da Silva Gomes Oliveira contributed in the conception, collection and analysis of data, writing and revision. **Patrícia Magnabosco** participated in the collection and analysis of data, writing and revision. **Juliana Pena Porto** collaborated in the conception.

How to cite this article (Vancouver)

Campos CS, Oliveira TSG, Anjos ACY, Ferreira MBG, Magnabosco P, Porto JP. Impact of fatigue on the quality of life of women with breast cancer. REFACS [Internet]. 2020 [cited in *insert day, month and year of access*]; 8(3):383-391. Available from: *insert access link*. DOI: *insert DOI link*.

How to cite this article (ABNT)

CAMPOS, C. S.; OLIVEIRA, T. S. G.; ANJOS, A. C. Y.; FERREIRA, M. B. G.; MAGNABOSCO, P.; PORTO, J. P. Impact of fatigue on the quality of life of women with breast cancer. REFACS, Uberaba, MG, v. 8, n. 3, p. 383-391, 2020. Available from: *insert access link*. Access in: *insert day, month and year of access*. DOI: *insert DOI link*.

How to cite this article (APA)

Campos, C.S., Oliveira, T.S.G., Anjos, A.C.Y., Ferreira, M.B.G., Magnabosco, P. & Porto, J.P. (2020). Impact of fatigue on the quality of life of women with breast cancer. REFACS, 8(3), 383-391. Retrieved in: *insert day, month and year of access* from *insert access link*. DOI: *insert DOI link*.