

## Association between Physical Activity, Pain and Fatigue in Patients undergoing Chemotherapy Treatment

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### Abstract

Chemotherapy patients have symptoms of pain and fatigue normally used as a justification for not performing physical activity during treatment. However, the association of these variables has not yet been conclusively performed in the studies. The aim of this study was to verify the association between physical activity, levels of pain and fatigue in chemotherapy patients. This was a quantitative, non-experimental and cross-sectional study. For oncological conditions and levels of physical activity, a semi-structured questionnaire was used; for fatigue the PFS-P was used; for pain, the EORTC-QLQ-C30 was used; and correlations were performed with the R-Spearman test ( $p < 0.05$ ). The sample consisted of 64 patients, of both sexes and without metastasis, with an age range of 31-80 years old. Of these patients, 26.57% practiced physical activity before the disease and 11.18% during chemotherapy. In assessing the pain variable, 30.7% of men and 74.51% of women had this symptom, with average score levels of 33 points. Regarding fatigue, 50% had this symptom, with a greater incidence in the affective dimension (7.99). The correlations between pain (-0.267) and fatigue (-0.265) with physical activity were negative. Thus, pain and fatigue were not related to the physical activity of patients undergoing chemotherapy.

**Key words:** Physical activity. Pain. Fatigue. Chemotherapy.

### INTRODUCTION

Cancer is the result of a disorderly growth of cells that invade tissues and organs. Dividing rapidly, these cells tend to be very aggressive and uncontrollable, determining the formation of tumors, which spread to other regions of the body<sup>1</sup>.

Malignant neoplasm is the second most diagnosed disease in the world. According to the World Health Organization (WHO), an estimated 46.1 million cases occurred in 2018, with 8.1 million deaths per year<sup>2</sup>. The National Cancer Institute (INCA) made a prognosis for the 2018-2019 biennium pointing out that

634,880 cases would be diagnosed, with the most prevalent types being prostate cancer (31.7%) and breast cancer (29.5%). For the state of Alagoas and the city of Maceió, the same institute indicated an estimate, respectively, of 5,050 and 1,840 cases<sup>3</sup>.

In recent years, cancer has come to be treated as a public health problem, having genetic conditions as a cause, as well as lifestyle, which includes high body mass indexes, physical inactivity, poor diet and stress<sup>4</sup>.

Treatment varies according to the degree of development of the disease and may

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include surgical procedures, radiation therapy, chemotherapy and pharmacological resources. Pain is reported as one of the side effects in the treatment of patients, which also includes fatigue, tiredness, nausea, vomiting, depression, asthenia, among others<sup>5</sup>. According to the International Association for the Study of Pain (IASP), pain is considered an “unpleasant emotional sensation or experience, associated with real or potential tissue damage”<sup>6</sup>, and can be considered as acute, chronic, neuropathic or mixed.

In cancer patients, pain symptoms, according to Mison (2012), may be associated with response to pharmacological treatment, invasive action of the neoplasm, other associated pathologies and psychosocial issues<sup>7</sup>. On the other hand, the practice of physical activity (PA) has been considered an important non-pharmacological resource to prevent the spread of neoplasms, to improve adverse reactions to cancer treatment and to acquire a better quality of life during and after surviving the illness<sup>8,9,10,11</sup>. Taking into account that pain can be used as a justification for not practicing PA by individuals in debilitating conditions, this investigation is justified by identifying the practice of movements as an essential adjuvant resource for the conditions of health and fatigue levels of patients undergoing cancer treatment.

In addition, fatigue is identified as the main side effect of treatment in 90% of cancer patients. This sensation can be defined as a tiredness condition that involves behavioral, emotional and cognitive elements, which promote effects such as drowsiness, low physical activity, disgust and unwillingness to continue performing tasks<sup>12,13</sup>. According to Masano-Schlosser (2014), for patients undergoing cancer treatment, fatigue contributes to the spread of depression, especially due to pain, physical disfigurement and loss of autonomy<sup>14</sup>.

In this sense, PA is also understood to be an auxiliary treatment in cancer patients.

The present study aimed to verify the relationship between the incidence of pain, the level of fatigue and the practice of physical activity in patients undergoing chemotherapy treatment at a public hospital in the city of Maceió, AL.

## METHODS

The study was characterized as an epidemiological study, with an analytical and cross-sectional methodology.

The target population were patients undergoing treatment at the High Complexity Oncology Center of a public hospital in the city of Maceió, Alagoas, between the months of July and August 2018.

The inclusion criteria established were: not being in the metastasis stage and being over 18 years old. Patients who were not in physical or psychological conditions to answer the questionnaires did not participate in the study.

The probabilistic sampling method was used to represent the target population. In this case, we chose a simple random sampling, respecting the representativeness of 20% of the population. At the end of the two-month period, 258 patients were seen at that hospital in the chemotherapy sector. A total of 64 patients were contacted in the chemotherapy waiting room and agreed to participate in the study.

A semi-structured questionnaire was applied, not validated and built by the researchers in order to acquire information about the oncological, social profile and the regular practice of PA by the patients before and during the chemotherapy treatment.

To assess pain, items 9 and 19 of the quality of life questionnaire were used for patients undergoing chemotherapy treatment from

The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC-QLQ-C30). This questionnaire is divided into three dimensions: functional symptoms, general symptoms and specific symptoms. Pain is verified in the dimension of general symptoms<sup>15</sup>. Scores were calculated separately for each of the scales, ranging from 0 to 100. On the global health and functionality scale, the higher the score the better the quality of life, while on the symptom scales the higher the amount of points are the worse the score<sup>15</sup>.

The Piper Fatigue Test (PFS-P), composed of 23 questions, was used to identify patients' fatigue levels. The scale assesses the individual's affective, sensory, cognitive and behavioral level, with each question scaled using a score from 0 to 10. The first question corresponded to the absence of fatigue; where 1 to 3 was an average level of fatigue, 4 to 6 moderate level of fatigue, and above 7 was considered a severe level of fatigue<sup>16,17,18</sup>.

The aforementioned questionnaires were applied by a single researcher in the hospital's chemotherapy waiting room on random days. During the two months of the collection, the researcher was in that environment for three days every week in the morning.

All patients signed the Informed Consent Form (ICF) authorizing the use of the information in the study. The research was approved by the Research Ethics Committee at the Federal University of Alagoas (UFAL) under the number of Opinion N°. 3.45.770/2019 concerning the project "Effects of Physical Exercise on Fatigue and Quality of Life in Cancer Patients" which is in progress.

For the analysis of data on the association between variables, statistical treatment was used in the SPSS for Windows program, version 2.1. In the isolated variables, the frequency distribution table was used. Moreover, to

analyze the association between the practice of physical activity, pain and fatigue, the Spearman's R correlation was performed, having  $p < 0.05$  as the reference value for significance.

## RESULTS

64 patients participated in the study - 51 women (79.7%) and 13 men (20.7%) - undergoing chemotherapy treatment at the public hospital. There was no exclusion of any type of participant at the beginning of the questionnaires. Table 1 shows the patients' profile data.

Concerning the age group, the range was between 31 and 80 years old. The incidence of treatment was perceived in people considered adults/young adults who represented 70.32% of patients, as opposed to the elderly (29.68%). The largest number of patients stands out for individuals aged between 41-50 years old.

With regard to the cancer profile for women, breast cancer was the reason for chemotherapy treatment for 48.43% of patients; followed by cervical cancer at 7.9%.

Many patients undergoing chemotherapy were diagnosed with neoplasms for less than one year (42.18%), which when added to those who were diagnosed more than 12 months earlier, results in a percentage of 71.86% patients with less than 2 years of diagnosis.

Regarding other associated diseases, females had a higher incidence, although a large part of this sample reported not having any disease other than a neoplasm (64.08%). It was noticed that chronic diseases, such as hypertension and type II diabetes, were the most recurrent. When we added them together, in both sexes, these types of pathologies reached a percentage of 18.74%.

The patients' practice of PA can be seen in Table 2. Before the diagnosis of the neoplasm, 17 patients (26.56%) practiced some type

of PA, as opposed to 47 (73.44%). In this scenario, women represent the largest portion (13). After the beginning of chemotherapy treatment, there was a moderate drop in patients who continued to perform some type of activity, those being 11 patients (17.18%), in contrast to the others (82.82%) who abandoned practicing PA.

The level of pain, perceived in the previous week by patients, varied according to gender, shown in Table 3. Only 30.77% of men reported feeling this symptom, in contrast to 74.51% of women, who mostly indicated being affected by a lot of pain (33.33%).

In one of the instrument's specific questions, it is possible to identify whether chemotherapy pain is the cause for the impediment of daily tasks. Concerning this item, it was found that 43.13% of women and 76.92% of men did not report having an association between pain and not performing daily activities.

Only 20 patients (31.25%) had scores above 50 points, indicating worrisome levels of pain correlated with quality of life.

The correlation between pain and the practice of PA can be seen from Table 4. In this sense, a negative correlation was noticed, that is, the increase in information about the manifestation of pain is not associated with the lack of practicing PA. An interesting example for those who practiced PA still under treatment (11 patients) was the incidence of a patient with above average scores (66 points); of six patients showing the existence of some type of pain (54.54%); and only four of these patients indicate pain hindering the performance of any daily task (36.37%).

For the variable fatigue (PFS-P), it was identified that half (n=32) of the patients consulted had suffered fatigue during the treatment. However, when asked about the duration of the fatigue, the results indicated that 31.25% of patients felt it for months and 28.15% for days.

In the dimensions of the instrument, patients presented the following results:

7.39 (behavioral); 7.99 (affective); 5.01 (psychosensory); and 6.27 (total score). Understanding that a score closer to 10 implies the patient had high fatigue, the dimension in which the sample had the greatest impact was in the affective dimension. However, in the sensory dimension, where the pain variable could be identified, the score was found to be at a moderate level.

The correlation between fatigue and the practice of PA can be seen in Table 4 and Figure 1. There was a significant difference in the levels of the overall score in the PFS-P among those who continued to practice PA (x-axis) during treatment and those who reported that they did not (figure 1). Only three of the 11 patients (27.27%) who were practicing activities reported still showing symptoms of fatigue (9.37).

An important variation between the fatigue scale scores is perceived between the groups: 0 to 7 (severe levels) for those who did not practice PA; and from 0 to 4 (moderate level) for those who practiced PA when it comes to PET. The greatest difference could be observed in the PDS where the group practicing PA had a minimum level of fatigue and the group not practicing was found having a moderate level of fatigue. The dimension that most seemed to affect patients who maintained their training routine was PDA, ranging from 0 to 4 (minimum to moderate level). Meanwhile, Table 4, in the correlation between Fatigue and PA, a decrease was observed in the most severe levels of fatigue according to the increase in the total number of samples who practice PA. This implies that the correlation between associated patients (who showed fatigue and those who did not report it) was negative, that is, the practice of PA is not related to the group with decreased sensations of this side effect of the chemotherapy treatment. Therefore, regardless of the practice of activity or not, patients pointed to satisfactory levels of fatigue even though they are under chemotherapy treatment.

**Table 1-** Profile of patients undergoing chemotherapy, Maceió - AL, 2019.

	<b>Variables</b>	<b>n</b>	<b>%</b>
<b>Sex</b>	Female	51	79.68
	Male	13	20.32
<b>Age Group</b>	30 to 40 years	11	17.18
	41 to 50 years	19	29.71
	51 to 60 years	15	23.43
	61 to 70 years	12	18.75
	71 to 80 years	7	10.93
<b>Type of neoplasm</b>	Breast	31	48.43
	Leukemia	7	10.93
	Cervical	5	7.81
	Lung	2	3.12
	Prostate	2	3.12
	Others	17	26.59
<b>Diagnosis Time</b>	Up to 1 year	27	42.18
	More than 1 year	19	29.68
	More than 2 year	8	12.52
	More than 3 year	10	15.62
<b>Associated Diseases</b>	Hypertension	4	6.25
	Type II Diabetes	4	6.25
	Hypertension + Type II Diabetes	3	4.68
	Bone and joint diseases	2	3.12
	Hypertension + Depression	1	1.56
	Others	9	14.06
	Does not have	41	64.08

**Table 2-** Practice of physical activity of patients undergoing chemotherapy, Maceió - AL, 2019.

Variables	n	%	
Practice of Physical Activity Before	No	47	73.44
	Yes	17	25.56
Practice of Physical Activity during Treatment	No	53	82.83
	Yes	11	17.17
Type of Physical Activity (before)	Walking	10	58.84
	Bodybuilding	1	5.88
	Dance	1	5.88
	Walking/ Running	1	5.88
	Soccer	1	5.88
	Walking + Bodybuilding	1	5.88
	Bodybuilding + Running	1	5.88
	Bodybuilding + Dance	1	5.88
Type of Physical Activity (treatment)	Walking	10	90.90
	Biking	1	9.10
Frequency (during treatment)	1-2 days	3	27.27
	3 days	5	45.46
	4 days	2	18.18
	Everyday	1	9.09
Duration time (treatment)	10-19 min	1	9.1
	20-29 min	4	36.36
	30-39 min	2	18.18
	More than 60 min	4	36.36

**Table 3-** Pain level of patients undergoing chemotherapy (EORTC-QLQ-C30), Maceió - Alagoas, 2019.

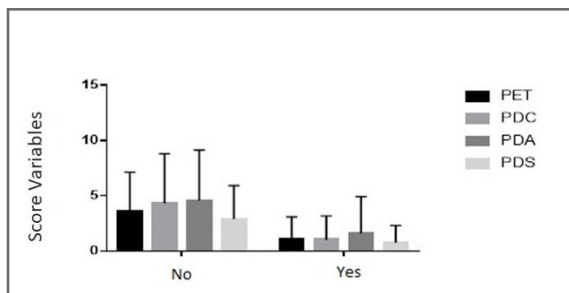
Variables	n	%	Variables	n	%
<b>Women</b>			<b>Men</b>		
None	13	25.49	None	9	69.23
Little	8	15.69	Little	3	2,07
Moderate	13	25.49	Moderate	1	7.7
A lot	17	33.33	A lot	0	0



**Table 4-** Correlation between physical activity, pain and level of fatigue in patients undergoing chemotherapy (Spearman's R), Maceió - AL, 2019.

Association	Spearman's R	P-value
Physical Activity / Pain	-0.267	0.037
Physical Activity / Fatigue	-0.265	0.034

**Figure 1-** Association between Physical Activity and the Fatigue Level of patients undergoing Chemotherapy Treatment (PFS-Piper), Maceió - AL, 2019.



Piper Total Score (PET); Piper Behavioral Dimension (PDC); Piper Affective Dimension (PDA) and Piper Psycho-sensory Dimension (PDS)

Mansano-Schlosser & Ceolim<sup>14</sup>, in their investigation in the chemotherapy outpatient clinics in Campinas, SP, with 140 individuals, identified 46.4% patients with some type of chronic disease reported. Although the sample numbers are different, this study dialogued with the scenario of the appearance of other pathologies during the chemotherapy treatment found here.

Regarding the type of PA of patients at the hospital in the city of Maceió, Alagoas, there was a greater incidence of cardiorespiratory activities, pointing to a tendency for patients to decrease the pace of body movements due to the impact of treatment. According to the literature, there is no counterindication to the practice of strength exercises for patients undergoing chemotherapy, as long as they are submitted

to training protocols with control of HRmax, VO2max and duration<sup>19</sup>.

Together with cardiorespiratory activities, it was noticed that the vast majority of patients performed PA for the minimum number of days recommended by WHO<sup>20</sup> for health components (45.46%). On the other hand, with regard to the duration of the PA, it was seen that patients have dedicated themselves to times above those recommended by WHO (90.9% of patients).

The levels and types of PA of patients at the public hospital in Maceió, Alagoas, in comparison with the recommendations proposed by Courtneya KS, Mackey JR & Jones LW (2000), are well below the desired levels. According to these authors, the preferred modalities would be those that work with large muscle groups; with a frequency of three to five times a week (except for chemotherapy intervention days); at a moderate intensity around 50 to 75% of VO2Max or HRreserve, or 60 to 80% HRmax; lasting 20 to 30 minutes, which can be progressive according to the patient's organic response, but long breaks for rest are necessary<sup>21</sup>.

According to the results found by Seixas<sup>22</sup>, with 38 patients, 63.2% of the patients had estimated levels of metabolic equivalent (MET) below 297, qualifying them as insufficiently active. This situation was also investigated by Mohammadi<sup>23</sup>, who pointed out, in Iran, that 65% of women practice low intensity PA. However, these results differ from that found by Templeton<sup>24</sup> with 342 women in Switzerland, where 69% identified themselves as active. Our results showed only 29.68% of the subjects performing PA could be qualified as active.

Finally, Kwan<sup>25</sup>, in the United States, with more than a thousand subjects, highlighted a decrease in the performance of PA in patients after six months of treatment. This situation reaffirmed the idea that patients, even if they performed some type of PA before treatment, abandoned the regularity of these practices

soon after the pharmacological action. Such a scenario is an indicative predictor for the incidence of the most severe side effects.

With regard to pain, Coucineiro, in his cross-sectional investigation with 267 cancer patients, detected that 53% of these patients had neuropathic pain, especially when there was a treatment associated<sup>26</sup>. In a cross-sectional and cohort study on the care management of 137 cancer patients in São Paulo, Mison managed to reduce the intensity of pain, through opioid manipulation, from 7.1 to 1.3 after the procedure<sup>7,11</sup>. The study by Ramos and collaborators corroborated the idea of using medication to control pain based on the recommendations of an “analgesic ladder” that ranged from the systemic identification of the clinical condition to the use of opioids<sup>27</sup>. Therefore, part of the studies on pain and cancer patients focus on the analysis of palliative care and relief of side effects during treatment, disregarding the possibilities of alternative and non-pharmacological therapies as aids in this process.

Vigário<sup>28</sup> in a study with patients undergoing thyroid cancer treatment used the SF-36 to assess quality of life after the intervention of an aerobic and strength exercise program over 12 weeks. It identified changes in the scores of emotional components, vitality and physical pain, as well as better results in WHOQOL-BREF in measurements of physical and psychological dimensions for those who were in the experimental group compared to the control group.

Meanwhile, Moros<sup>29</sup>, with 22 randomized women, based on a protocol of dynamic aerobic exercises, identified improvements in the dimensions of insomnia, pain and fatigue of the components of the EORTC-QLQ-C30 questionnaire. Although there was an improvement in the total score, both for the control group and for the experimental group, in

the latter there were higher responses. Thus, he demonstrated that although the disease leads to negative physiological effects, interventions can improve functional capacities.

Boing et al., studying 122 women with breast cancer in Florianópolis, SC, detected scores for pain when using EORTC-QLQ-C<sup>30</sup> in different types of treatment - chemotherapy (51.1), radiation therapy (30.9) and hormone therapy (34.5) - demonstrating that the chemotherapy groups showed greater responses to this variable<sup>30</sup>. The results found in the public hospital in Maceió, AL were closer to those found in the radiotherapy group in SC. Using the same instrument, Seixas, in an investigation with 38 subjects of both sexes, in RS, detected that there was no statistical difference ( $p=0.77$ ) in the pain variable, among patients who had MET's levels above or below 297<sup>22</sup>. This is different from what was presented in this study, in which patients who maintained their practice of PA pointed to lower scores in the pain dimension of the EORTC-QLQ-C30.

Regarding fatigue, many patients undergoing cancer treatment pointed out their symptoms, but were unable to understand this set of physiological responses to the organism subjected to pharmacological immersion. According to Mota<sup>18</sup>, the rate of patients with fatigue during treatment is extremely high. However, this side effect in patients is considered difficult to understand because it relates to several dimensions, acts in a complex way and has a variation of sensations for each individual.

Mota, in a study with 157 patients with colon cancer of the uterus, found that in 26% of the individuals had fatigue indexes, with higher scores for the areas of pain, impaired sleep, depression, impaired functional capacity and public health service. Based on the correlation of other instruments (Beck Depression Inventory, Pain Scale and Sleep Impairment School), he



pointed out that depression corroborated the increase in fatigue, functional capacity and quality of sleep of the patients.

Reis<sup>31</sup>, when studying the action of different physical exercise programs in 44 patients, found that aerobic exercises showed better results in patients' PFS-P scores, although in different protocols there were beneficial changes in the results after the intervention. Thus, after four months there was a decrease in the level of fatigue, making it an important aid to the treatment.

Meanwhile, Schiappacase<sup>32</sup>, from a multimodal therapy with 80 patients in Chile, noticed that, after the intervention with moderate aerobic exercises, there was an improvement in fatigue levels in 35 cases after only 2 weeks comparing those who used medication to control fatigue and exercised. Battaglini<sup>19</sup>, in a study with 27 patients in the relationship between physiological adaptations, PA and fatigue, identified that there was no improvement in physical fitness with the reduction of fatigue; rather, they was noticed that there was an improvement in other aspects of physical conditioning.

## CONCLUSION

It was concluded that part of the patients did not practice PA before their cancer diagnosis, and those who did, interrupted PA with the beginning of chemotherapy sessions. Pain cannot be considered as the justification for not performing and/or interrupting the practice of PA. The scores of the fatigue and quality of life instruments (pain component) pointed to favorable conditions for carrying out daily tasks, independently of pain. Thus, other elements could be responsible for the

Therefore, patients undergoing chemotherapy treatment at a public hospital in the city of Maceió, AL showed standard behavior regarding side effects linked to fatigue. However, in the sample group that maintained PA, it seemed to have produced a decrease in the PFS-P scores, although the association in the total group did not reach a positive correlation.

In terms of study limitations, the small sample size that may not represent the total group of patients being treated at the institution should be highlighted. In addition, the difference in the number of participants did not allow for a thorough analysis between the sexes. Another important element to highlight is the characteristics that involve the application of questionnaires. Such data may vary according to the researcher's approach, the level of satisfaction for contributing to the data collection, the patients' mood on the day the questionnaire was filled out and their state of mind in relation to the pathology. This time, the information presented more likely identifies a group's trend at a specific time during chemotherapy treatment.

abandonment of regular practice of PA by patients undergoing chemotherapy, such as tiredness, lack of disposition, depression and, even, ignorance of the role of PA in improving health conditions before, during and after the treatment. Campaigns, conversations and other policies should be carried out to overcome the psychological barriers that prevent the adoption of active behavior by these patients; especially those who are still in conditions in which they can perform lifestyle changes.

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