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Physical activity and levels of fatigue in cancer patients

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ABSTRACT

Purpose: The purpose of this study was to correlate physiological adaptations caused by physical activity and levels of fatigue in cancer patients. **Methods:** Twenty-seven cancer patients (56.67 ± 14.82 years old) who have been treated with chemotherapy, radiation or the combination of both treatments, were voluntary for this study. All patients were submitted to pre-exercise and post-exercise physical assessment. During the physical assessment a questionnaire measuring levels of fatigue was applied (Piper *et al.* 1989). All independent variables (physiological adaptations) were standardized (Z scores). According to the multiple regression linear models, all variables were analyzed simultaneously. **Results:** The results did not show any significant ($p < 0.05$) relationship between reduction in fatigue and improvement in physical fitness ($r^2 = 0.102$). The multiple linear regression analysis and the simple correlation results were not significant. **Conclusion:** Although there was no significant correlation between improvement in physical fitness and reduction of fatigue, the relationship between fatigue and physical fitness was linear and positive.

Key words: Aerobic exercise. Resistance training. Cancer treatment.

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INTRODUCTION

According to the United States Cancer Institute[1], from 72% to 95% of cancer (CA) patients under treatment presented an increase on the levels of fatigue resulting in a significant decrease on the functional capacity, leading to a great health loss in the quality of life. A study[2] revealed that due to the high levels of fatigue: a) 71% of patients under treatment missed one day or more of work per month; b) 31% missed at least one week; and c) 28% resigned from their jobs. It was also verified in this research that many of the patients had trouble on simple daily activities like going shopping (56%), doing simple cleanings in their own houses (31%), going upstairs (56%), and doing strolls a little longer (69%).

The metabolism of cancer patients suffers drastic modifications due to the stress caused by the disease itself as well as by the side effects produced by the traditional treatments (surgery, chemotherapy or radiation). The combinations of these metabolic modifications may be associated to the psychological depression and to the appetite reduction, factors that lead patients to start a vicious cycle of muscular mass loss and decrease on the physical activity, resulting in a generalized weakness status[3].

The physical activity produces chronic metabolic and morphological alterations that may become an important choice for the treatment and for the recovery process involving cancer patients[4]. However, not many researches are being currently conducted involving the use of physical activities on the rehabilitation of cancer patients.

Some rehabilitation-specialized centers in the United States have used different physical exercises programs on the recovery of these patients[5]. Such programs have as main objective the improvement of the cardiovascular capacity, the reduction on the body fatness, and the increase on the muscular strength, power and flexibility. All these associated factors decrease the harmful alterations on the metabolism, thus improving the health and the quality of life of patients, bringing a better expectancy on the struggle against the disease.

Recently in a revision study, Courneya[3] reported that when studies of breast cancer and exercise are excluded, only 10 studies had investigated the effects of the exercises during the treatment of patients with several types of cancer. However, only one of these studies[4] approached the correlation between physical fitness and fatigue.

The volume, intensity and the types of physical exercises are the main factors that should be taken into consideration to the prescription of exercises specific for cancer patients be successful. Currently, shortly after the diagnosis of the disease, different prescription approaches have been used as treatment model. These physical exercises were applied along with the administration of traditional cancer treatments (surgery, chemotherapy or radiation), being also applied after the end of such treatments[2,6-10]. However, many of the chronic alterations induced by the exercises may not bring benefits to the levels of fatigue of these patients. Therefore, the chronic adaptations induced by the exercise and its relations with the level of fatigue should be better established.

The objective of this study was to correlate physiological adaptations caused by physical activity and the levels of fatigue in cancer patients submitted to treatments involving chemotherapy, radiation or the combination of both treatments.

MATERIAL AND METHODS

Sample

Twenty-seven cancer patients submitted to surgery, chemotherapy and radiation were voluntary in this project. From this total, only two men (one of them with colon cancer and the other with prostate cancer) and the other 25 were women as follows: one woman with cerebral cancer, two with thyroid cancer and 22 with breast cancer. For this study, we did not select patients according to the type of cancer, and all were included into the same group. The average age among patients was 56.6 years, ranging from 24 to 78 years old. The patients were recruited in the Northeast region from the State of Colorado, United States. An informative official report containing information about the objectives of the study, methods of data collecting, methods of data analysis and details for the participation on the project was distributed to all participants.

The exclusion criterions for the participation on the project included: cardiovascular problems, metastasis, acute or chronic respiratory problems, cognitive dysfunction and immunologic deficiency. Explanations regarding the protocols, objectives, risks and the right to quit the participation were given during the first visit of the patient after the diagnosis of the disease. The patients selected signed up an approval form before beginning the study. This study was approved by the ethics committee for researches involving humans from the University of Northern Colorado (UNC).

Measures procedures

The physiological parameters evaluated (independent variables) included:

1) Cardiovascular capacity – The alterations on the aerobic resistance were analyzed through the duration time of a submaximal effort test (75% of the cardiac frequency maximal-FC_{max}) in ergometer treadmill. The volunteers were submitted to a treadmill ergometry test, according to the recommendations of the modified Bruce protocol, aiming at the establishment of the cardiac frequency. The equipment used for the analysis of the cardiovascular efficiency was a *Quinton* (model 3000) equipped with electrocardiogram and treadmill (model 65). The cardiac frequency was verified at the resting phase and at the end of each minute of the test stages, with duration of three minutes each and at all the recovery phase, which lasted as long as three minutes using a frequencymeter *Polar* model *Accurex Plus (USA)*. The test was interrupted when patients reached 75% of the maximal cardiac frequency, calculated through the formula of Karvonen. This interruption was necessary due to the patient's fatigue degree.

2) Muscular strength – In the analysis of the muscular strength, the protocol used was the adapted *Dynamic Muscular Endurance Test*[11]. The adaptation in the protocol was performed by the Rocky Mountain Cancer Rehabilitation Institute, UNC. The adaptation was necessary due to the lack of power in cancer patients for performing the loads stipulated in the original protocol. For this reason the load percentages in relation to the body mass were reduced (table 1). The equipments used were *Life Fitness* and *Quantum*.

3) Flexibility – For the analysis of the flexibility, the protocol used was the modified "sit and reach" test[12].

TABLE 1
Body mass percentage values to establish the load of work of each exercise, according to gender and age

Exercise	Age: < 45	Age: 45-60	Age: 60-70	Age: > 70
Leg press				
Men	0.650	0.610	0.580	0.550
Women	0.525	0.485	0.455	0.425
Supine				
Men	0.500	0.470	0.440	0.410
Women	0.375	0.350	0.330	0.310

4) Body composition – In the evaluation of the body composition, the protocol of "three skinfolds" of Jackson *et al.*[14] for women was used.

5) Resting cardiac frequency (FCr) – The FCr was examined after the patient remained in rest during 15 minutes, through the use of a cardiac frequency monitor *Polar®*. The FCr was measured at the same timetable and alimentary conditions for all patients.

6) Levels of fatigue – For the analysis of the levels of fatigue, the questionnaire measuring levels of fatigue revised by Piper *et al.*[15] was used. The questionnaire measuring levels of fatigue (dependent variable) consists of 22 items subdivided into four different subjective domains of fatigue measures: affective, sensorial, cognitive and behavioral.

Training

All patients participated on two physical evaluations, one before the beginning of the physical exercises and other six months later. Before the beginning of the physical evaluations, the patients responded to the questionnaire measuring levels of fatigue revised by Piper *et al.*[15]. The duration of the physical exercises program was of 24 weeks. The patients participated on two physical activities session per week (on Tuesdays and Thursdays) with one day of rest between sessions.

The design of the physical exercise sessions included: from 5 to 10 minutes of elongation; from 10 to 20 minutes of treadmill or cycle ergometer (50% to 55% of the FC_{max}); resistance exercises (lateral and frontal development with horizontal supine dumbbell, use of the *pulley*, *leg press*, knee flexion and extension and abdominal exercises). At the end of each session, 5 to 10 minutes of elongation were performed.

The weight exercises were performed at 50% of a maximal repetition (1RM) with one series of each exercise in the first four weeks and two series in the following weeks. Progressive intensities were applied according to the recommendations of the progression model from the American College of Sports Medicine (ACSM) for muscular strength training[16]. Each patient had an exercise specialist at his disposal during the entire study. The specialists were trained by the Rocky Mountain Cancer Rehabilitation Institute (RMCRI) from the University of Northern Colorado.

In order to the statistical analysis of correlation between the results of the improvement on the physiological parameters analyzed (independent variables) and the results of the improvement on the fatigue reduction (dependent variable) be performed, the following steps were taken: firstly, all post-test results of resting cardiac frequency, fatness percentage, total time at treadmill, maximum number of repetitions in endurance exercises, flexibility level and the result of the questionnaire measuring levels of fatigue revised by Piper *et al.*[15] were subtracted from the results obtained in the first evaluation (pre-test) of the same variables. Considering that the decrease on the results of the resting cardiac frequency measures and the fatness percentage mean improvements on these parameters, the subtraction results were multiplied by minus one (–1). Improvements on the score of the questionnaire measuring levels of fatigue[15] represent a decrease on the patient's fatigue state. For that reason, the subtraction results were also multiplied by minus one (table 2).

The second step in the statistical analysis after the rearrangement of the values obtained for each variable was the standardization of the values obtained for the independent variables (Z scores), thus enabling the comparative analysis between these variables. According to the non-normal distribution of the dependent variable (fatigue reduction – skewness = 3.34), this variable was also standardized for Z scores.

TABLE 2
Non-standardized values of the initial (pre-test) and final (post-test) differences of the dependent and independent variables (n = 27)

Variable	Pre-test	Post-test	Δ
% Fatness	28.69 ± 7.85	27.91 ± 7.62	0.78
FCR (bpm)	79.62 ± 13.70	73.55 ± 8.48	6.07
Treadmill time (min)	5.86 ± 2.17	7.60 ± 2.07	–1.74
Supine (repetitions)	7.66 ± 9.36	18.59 ± 10.53	–10.92
Leg press (repetitions)	9.56 ± 7.34	23.40 ± 13.83	–13.85
Abdominal (repetitions)	25.11 ± 15.44	42.37 ± 24.27	–17.26
Flexibility (inches)	10.83 ± 3.69	12.19 ± 2.47	–1.37
Scale of fatigue (Piper *et al.*, 1989)	5.51 ± 4.06	2.39 ± 2.01	3.12

Where: Δ = Pre-test – post-test.

TABLE 3
Sample initial characteristics (n = 27)

Variable	Average ± SD	Amplitude
Age (years)	56.67 ± 14.82	24.00-78.00
% Fatness	28.69 ± 7.85	14.00-43.94
FCR (bpm)	79.62 ± 13.70	60.00-120.00
Treadmill time (min)	5.86 ± 2.17	1.17-10.09
Supine (repetitions)	7.66 ± 9.36	0.00-40.0
Leg press (repetitions)	9.56 ± 7.34	0.00-20.00
Abdominal (repetitions)	25.11 ± 15.44	0.00-75.00
Flexibility (inches)	10.83 ± 3.69	0.00-16.50
Scale of fatigue (Piper *et al*., 1989)	5.51 ± 4.06	0.00-24.00

Where: SD = Standard deviation; FCR = Resting cardiac frequency.

With the objective of testing the correlation between the independent variables and the dependent variable, the data analyses were performed by means of a multiple linear regression. According to the non-significant result of correlation between the independent variables in the model, where only a slight correlation between the independent variables, resting cardiac frequency and horizontal supine exercise was verified, it was suggested the creation of an independent variable involving the combination of all physiological parameters in the model for correlation analyses with the dependent variable fatigue reduction. After presenting a non-significant result in this last mentioned analysis, the employment of a *post-hoc* using univariable correlations had only and exclusively descriptive purposes.

The last step in the data statistic analysis involved the analysis of a univariable correlation including the correlation between the combination of all standardized results of the independent variables with the result of the dependent variable.

RESULTS

The table 3 shows the initial characteristics of the variables analyzed from volunteers at the beginning of training. As shown by table 1, the sample used in the present study showed a characteristic quite heterogeneous. The initial average age of volunteers was 56.7 ± 14.8 years and the relative fatness was 28.7 ± 7.8% G.

The analyses performed through the multiple linear regression model involving the combination of all independent variables (reduction on the resting cardiac frequency, reduction on the fatness percentage, improvement on the result of the treadmill submaximal test – total time at treadmill, improvement on the horizontal supine exercise, leg-press, abdominal and flexibility) and the dependent variable (the result of improvement on the questionnaire measuring levels of fatigue revised by Piper *et al.*[15] showed a non-significant correlation ($r = 0.32$; $r^2 = 0.102$) (table 4).

TABLE 4
Multiple regression between reduction of fatigue and improvement of physiological parameters (n = 27)

Independent variables	Dependent variable (reduction of fatigue)	*p*
R^2	0.102	0.941
Intercession	0.979	0.740
% Fatness	0.090	0.710
FCR (bpm)	0.233	0.401
Treadmill time (min)	0.111	0.663
Supine (repetitions)	–0.040	0.876
Leg press (repetitions)	0.118	0.642
Abdominal (repetitions)	0.196	0.449
Flexibility (inches)	–0.108	0.656

p = level of significance.

The results of the analysis of univariable correlations in agreement with the results presented through the analysis of multiple linear regression also presented non-significant results.

The independent variables that demonstrated a positive correlation, although non-significant, with the reduction on the level of fatigue of patients were (from the strongest correlation to the weakest correlation): improvement on the resting cardiac frequency, abdominal exercise, leg-press exercise and reduction on the fatness percentage (table 5).

The result of the univariable correlation between the combination of all standardized results of the independent variables (Z scores) with the standardized result of the dependent variable (Z scores) are presented on figure 1. The result of this combination was positive although non-significant ($r^2 = 0.183$, $p = 0.351$).

TABLE 5 Univariable correlation between reduction of fatigue and improvement of the physiological parameters (n = 27)			
Variable	**Correlation (r)**	**r²**	***p***
% Fatness	0,104	0,056	0,60
FCR (bpm)	0,186	0,035	0,34
Treadmill time (min)	0,001	0,00	1,00
Supine (repetitions)	–0,034	0,011	0,86
Leg press (repetitions)	0,123	0,015	0,53
Abdominal (repetitions)	0,180	0,004	0,36
Flexibility (inches)	–0,048	0,002	0,81

p = level of significance.

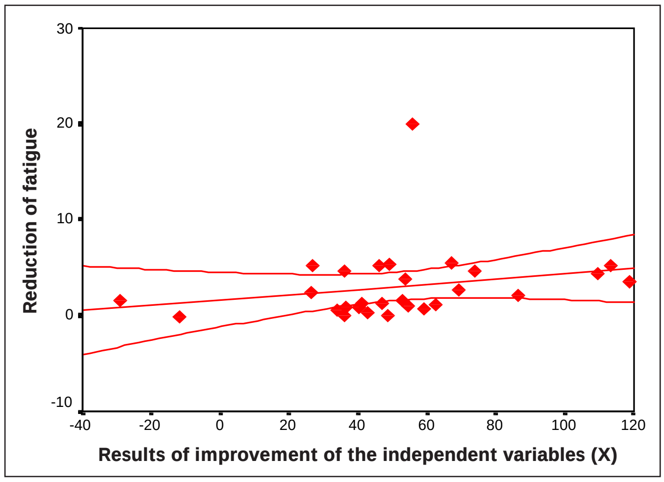

***Fig. 1** – Reduction of fatigue (Y)* vs *combination of the independent variables (X)*

DISCUSSION

The conception of applying physical exercises used with the objective of aiding cancer patients on the reduction of fatigue, which is caused by traditional treatments, not always is accepted as a viable and important choice for the recovery of the patient. Many patients would disagree with the idea of participating on rehabilitation programs involving physical exercises, once many of them are already found in deep physical debility state and unable to participate even on simple daily tasks. Countless studies have suggested the use of physical exercises on the rehabilitation of cancer patients due to their several benefits[2,6,17-21]. Some of these benefits include: improvements on the cardiovascular, respiratory and muscular systems through the improvement on the oxygen intake, muscular vascularization, motive coordination and balance, strength and improvement on the lymphatic circulation[21]. The side effects caused by conventional treatments leave long-lasting sequels, involving several biological systems. Many researchers have suggested that these side effects could be minimized or reverted through the use of physical exercises[20,21].

The aerobic activities, defined as contraction rhythmic activities and relaxation of large muscular groupings during a long period of time, have been quite efficient on the improvement of the aerobic capacity of cancer patients[3,4]. In a study conducted by Dimeo *et al.*[4], the most relevant result was the verification that the patients were reducing the level of fatigue and returning to regular daily activities with no limitations. Although rehabilitation programs for cancer patients traditionally use aerobic activities as the main type of physical activity, researches have suggested the use of a combination of weight and aerobic works, when these patients are individually prescribed and supervised, or only the performance of weight exercises[9,10]. Still, preceding studies involving the combination of these two different types of exercises would have emphasized a larger utilization on the quantity of aerobic activities if compared to the strength exercises[9]. Thus, many of the benefits that could have been provided through the participation on strength activities could not be established.

The main objective of the present study was to establish the relationship between the results of different types of physical exercises, analysing improvements on different physiological parameters, on the reduction of fatigue in cancer patients. The non-significant result of the correlation between the improvement on the general physical conditioning and the reduction of fatigue in this study could have been attributed to the low number of participants. Still, the analysis of univariable correlations demonstrated different results on the correlations between the physiological parameters separately analyzed and the fatigue reduction. The results of these correlations show that the improvement on the resting cardiac frequency, abdominal exercise, leg-press and the reduction on the fatness percentage were the physiological parameters that most contributed to the fatigue reduction of patients. The improvement on the treadmill test (total treadmill time) demonstrated a null correlation with the fatigue reduction, result that does not agree with preceding researches[4,7].

Researches involving cancer patients are quite complexes. Among the main factors are the limitations as high mortality levels, low number of participants willing to participate, different types of cancer treatments and different types of cancer. Although the low number of participants had been the main limitation of the present study and of the non-significance of the statistical values of the correlation between the general improvement of the patient's physical condition (results of improvement of the independent variables – physiological parameters combined as one single variable) as well as the reduction on the level of fatigue (improvement on the result of the questionnaire measuring levels of fatigue revised by Piper *et al.*[15]), these variables presented a quite positive and linear informative correlation standard. The positive and linear correlation observed between these variables suggests that the improvement on the several physiological parameters, and not only of a single parameter exclusively, causes a positive influence on the reduction of fatigue in cancer patients.

The positive and linear correlation between the improvement on the general physical conditioning and the reduction on the levels of fatigue presented in this study also serve as basis for further investigations that would have the objective of reproducing this study in order to verify whether this positive and linear standard between physical activity and fatigue would repeat in a study involving a larger and more homogeneous sample of cancer patients.

Furthermore, as patients could not present immunologic deficiency in order to participate in this study, it is suggested a better follow-up of the hemoglobin levels for further studies, once these levels may influence the training improvement and especially the levels of fatigue.

The results of this study enable new researching lines in the cancer field and physical exercises prescribed as physical rehabilitation for cancer patients. Questions such as:

- What type of physical exercise would be the most effective on the rehabilitation of cancer patients (aerobic activity, weight exercises or the combination of both with emphasis to the strength activity)?
- Would the quantity and intensity of exercises used in the present study be actually sufficient for a satisfactory physiological response on the reduction of fatigue?
- Could the positive and linear result, presented in the correlation between physiological parameters and reduction of fatigue, be repeated in further investigations involving a larger number of participants?
- Would different types of exercises bring different physiological responses in patients with different types of cancer?

CONCLUSION

Currently, there has been a progressive interest on the possibility that physical exercises improve health in the quality of life, also increasing the life expectancy for cancer carriers. Nevertheless, studies in this area are not yet quite conclusive, with several methodological limitations. Therefore, it is expected that the results of this work, even though with the limitations already mentioned, come to improve the scientific knowledge and serve as basis for further investigations involving physical activities used as physical rehabilitation for cancer patients.

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