Analysis of Reported Fatigue and of Respiratory and Peripheral Muscle Strength in Individuals with Cancer Undergoing Treatment

doi: https://doi.org/10.32635/2176-9745.RBC.2020v66n4.1051

Análise da Fadiga Relatada e das Forças Musculares Respiratória e Periférica em indivíduos com Câncer em Tratamento

Análisis de la Fatiga Reportada e de las Fuerzas Musculares Respiratoria y Periférica en Individuos con Cáncer Sometidos a Tratamiento

Karina Oliveira Prado Mariano[1]; Ricardo da Silva Alves[2]; Ana Paula Aparecida Mantuani[3]; Sabrina Rosse Carvalho[4]; Carmélia Bomfim Jacó Rocha[5]; Denise Hollanda Iunes[6]; Juliana Bassalobre Carvalho Borges[7]; Leonardo Cesar Carvalho[8]

ABSTRACT

Introduction: In recent years, cancer treatment has evolved, allowing longer survival for the patient, but, side effects such as a decreased immunity and fatigue influence the respiratory and muscular systems. **Objective:** Analyze fatigue, the respiratory and peripheral muscle strength in individuals with cancer undergoing treatment and in healthy individuals. **Method:** Analytical, observational, cross-sectional, and controlled study. The individuals were divided into two groups: a cancer group in chemotherapy and/or radiotherapy (CAG: n = 98; men = 35.72%; women = 64.28%; age = 58.13 ± 13.26 years; body mass index (BMI) = 26.23 ± 4.04 kg/m^2; time of cancer diagnosis = 27.54 ± 9.61 months) and a control group (CG: n = 86; men = 30.23%; women = 69.77; age = 59.24 ± 12.87 years; BMI= 26.76 ± 4.04 kg/m^2). For all the individuals, the reported fatigue was assessed using the fatigue subscale of The Functional Assessment of Cancer Therapy-Fatigue (FACT-F) questionnaire. The evaluation of maximal respiratory pressures was performed by manovacuometry and the palmar grip strength by manual dynamometry. **Results:** The CAG showed the highest reported fatigue index (p<0.001; f^2=0.382), lower values for respiratory variables (PImax: p<0.001; f^2=0.441; PEmax: p<0.001; f^2=0.361), left palmar grip strength (p=0.024; f^2=0.182), when compared to the CG. **Conclusion:** Volunteers with cancer in chemotherapy and/or radiotherapy presented higher levels of reported fatigue, with reductions in respiratory muscle strength and palmar grip strength.

Key words: Neoplasms; Muscle Strength; Muscle Fatigue; Breath Tests; Rehabilitation.

RESUMO

Introdução: Nos últimos anos, o tratamento do câncer evoluiu, possibilitando uma maior sobrevida ao paciente, porém os efeitos colaterais, como a diminuição da imunidade e a fadiga, influenciam o sistema respiratório e muscular. **Objetivo:** Analisar a fadiga e as forças musculares respiratória e periférica em voluntários com câncer em tratamento e em indivíduos saudáveis. **Método:** Trata-se de um estudo analítico, observacional, transversal e controlado. Os indivíduos foram distribuídos em dois grupos: um grupo de câncer em quimioterapia e/ou em radioterapia (GCA: n=98; homens=35,72%; mulheres=64,28%; idade=58,13±13,26 anos; índice de massa corporal (IMC=26,23±4,04 kg/m^2; tempo de diagnóstico de câncer=27,54±9,61 meses) e um grupo controle (GC: n=86; homens=30,23%; mulheres=69,77; idade=59,24±12,87 anos; IMC=26,76±4,04 kg/m^2). Para todos os indivíduos, a fadiga relatada foi avaliada, usando-se a subescala de fadiga do questionário *The Functional Assessment of Cancer Therapy-Fatigue* (FACT-F). A avaliação das pressões respiratórias máximas foi realizada por meio da manovacuometria e da força de preensão palmar por intermédio da dinamometria manual. **Resultados:** O GCA apresentou maior índice de fadiga relatada (p<0,001; f^2=0,382), valores inferiores para as variáveis respiratórias (PImax: p<0,001; f^2=0,441; PEmax: p<0,001; f^2=0,361), força de preensão palmar esquerda (p=0,024 f^2=0,182), se comparado ao GC. **Conclusão:** Voluntários com câncer em quimioterapia e/ou em radioterapia apresentaram maiores níveis de fadiga relatada, com reduções da força muscular respiratória e da força de preensão palmar.

Palavras-chave: Neoplasias; Força Muscular; Fadiga Muscular; Teste respiratórios; Reabilitação.

RESUMEN

Introducción: En los últimos años, el tratamiento oncológico ha evolucionado, permitiendo una supervivencia más larga para el paciente, pero los efectos secundarios como la disminución de la inmunidad y la fatiga influyen en los sistemas respiratorios y musculares. **Objetivo:** Analizar la fatiga e las fuerzas musculares respiratoria y periférica en individuos con cáncer sometidos a tratamiento y en individuos sanos. **Método:** Se trata de un estudio analítico, observacional, transversal y controlado. Los individuos fueran divididos en dos grupos: un grupo de cáncer bajo quimioterapia y/o radioterapia (GCA: no 98; hombres 35,72%; mujeres 64,28%; edad 58,13±13,26 años; indice de masa corporal (IMC) a 26,23±4,04 kg/m^2; diagnóstico de cáncer 27,54±9,61 meses) y un grupo de control (CG: no 86; hombres 30,23%; mujeres 69,77; edad de 59,24±12,87 años; IMC 26,76±4,04 kg/m^2). Para todos los voluntarios, la fatiga notificada se evaluó utilizando la subescala de fatiga del cuestionario *The Functional Assessment of Cancer Therapy-Fatigue* (FACT-F). La evaluación de las presiones respiratorias máximas se realizó mediante manovacuometría y fuerza de agarre palmar mediante dinamometría manual. **Resultados:** El GCA tuvo el índice de fatiga notificado más alto (p<0,001; f^2=0,382), valores más bajos para las variables respiratorias (PImax: p<0,001; f^2= 0,441; PEmax: p<0,001; f^2=0,361), fuerza de agarre palmar izquierda (p=0,024; f^2=0,182), en comparación con el GC. **Conclusión:** Voluntarios con cáncer en quimioterapia y/o radioterapia presentaron mayores niveles de fatiga reportados, con reducciones en la fuerza muscular respiratoria y fuerza de agarre palmar.

Palabras clave: Neoplasias; Fuerza Muscular; Fatiga Muscular; Pruebas Respiratorias; Rehabilitación.

[1]Department of Physiotherapy of the Foundation of Teaching and Technology of Alfenas of the University José do Rosário Vellano (UNIFENAS). Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0003-3007-2833

[2]College of Physiotherapy of the University of Vale do Sapucaí (Univás). Program of Post-Graduation of Biosciences applied to health. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0001-6931-3943

[3]Institute of Sciences of Motricity of the Federal University of Alfenas (UNIFAL). Program of Post-graduation in Sciences of Rehabilitation. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/000-0002-5989-8981

[4]Institute of Sciences of Motricity of UNIFAL. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/000-0002-5989-8981

[5]Institute of Sciences of Motricity of UNIFAL. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0002-7819-5683

[6]Institute of Sciences of Motricity of UNIFAL. Program of Post-Graduation of Sciences of Rehabilitation. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0003-1396-9980

[7]Institute of Sciences of Motricity of UNIFAL. Program of Post-Graduation of Sciences of Rehabilitation. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0003-0868-717X

[8]Institute of Sciences of Motricity of UNIFAL. Institute of Sciences of Motricity of UNIFAL and Biosciences applied to Health. Alfenas (MG), Brazil. Orcid iD: https://orcid.org/0000-0001-6511-8315

Corresponding author: Karina Oliveira Prado Mariano. Rua Salvador Quesada, 65 – Jardim Aeroporto. Alfenas (MG), Brazil. CEP 37130-804. Email: drakarina@bol.com.br

This article is published in Open Access under the Creative Commons Attribution license, which allows use, distribution, and reproduction in any medium, without restrictions, as long as the original work is correctly cited.

INTRODUCTION

Cancer is considered a chronic disease, one of the main causes of death and obstacle to increase life expectancy worldwide in the XXI[1] century. In Brazil, incidence and mortality by cancer increased while in the developed countries, even with raising incidence, mortality reduced[2].

Overall, surgery is the treatment for several types of cancer followed by chemotherapy and/or radiotherapy and/or hormone therapy and/or immune therapy[3]. The effects of these treatment modalities induce the increase of cytokines activities that lead to changes as sarcopenia, cachexia, increase of muscle fatigue[4,5]. The activation of these factors provoke modifications of the muscle protein metabolism, increasing the derangement and decline of the synthesis, which can predispose to reduce the ability to generate muscle strength[6].

The peripheral muscle strength can be evaluated through the test of palmar grip strength and is being utilized to determine the frailty, relating it to muscle global fatigue[7,8] and as marker of prognosis of mortality across several age-ranges[9]. Some studies suggest that the presence of fatigue can reflect in compromise of peripheral muscle and respiratory muscle strength[10-12].

One of the main effects caused by chemotherapy and radiotherapeutic treatment is the cancer-related fatigue (CRF), affecting 95% of the patients[13], can remain for months to years after its conclusion[4]. CRF according to the National Comprehensive Cancer Network is defined as a "distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning"[5]. Some studies have demonstrated that patients with cancer in different stages of the treatment present, in addition to CRF[14,15], reduction of the peripheral muscle strength[16], as the muscles of the leg[14] and of the middle deltoid muscle[15].

The treatments of the different types of cancer can provoke damages to the epithelial tissue, reduction of the inspiratory capacity and of the vital capacity, interfering in the pulmonary volume and in the respiratory muscle strength[17,18]. The presence of the CRF can negatively impact the functioning of the respiratory system too, causing ventilatory dysfunction[19]. In addition, chemotherapy can contribute for the onset of neurologic symptoms[20]. Radiotherapy favors mobility restraints, reduction of the capacity to contract the respiratory muscles and consequent alteration of the respiratory pressures[17,21] and pulmonary volume[17].

A useful method for the evaluation of the maximum respiratory pressures is manuvacuometry, since the maximum inspiratory pressure (MIP) is clinically relevant because inspiratory muscles support bigger loads of ventilatory work. The measurements of MIP and of the maximum expiratory pressure (MEP) are useful to differentiate the abdomen neuromuscular weakness and a specific frailty of the diaphragm or other respiratory muscles[22].

Another factor related to the accentuation of the perception of fatigue may have been attributed to the orientations of health professionals who encourage the patients to remain in rest during and after treatment[23,24]. In this sense, the present study attempts to offer a better understanding about the fatigue reported, the peripheral muscle strength and the respiratory muscle strength in volunteers with cancer in treatment compared with volunteers without cancer.

METHOD

Clinical, observational, cross-sectional and controlled study approved by the Institutional Review Board of the Federal University of Alfenas (UNIFAL), MG, number 1.980.365, conducted from August 2016 to April 2018. All the volunteers were briefed about the objectives of the study and signed the Informed Consent Form.

The sample was assigned by convenience divided in two groups: volunteers with cancer in treatment (CAG) and volunteers without cancer – control group (CG). CG consisted of companions of patients who were in the physiotherapy clinic randomly enrolled through an invitation to join the study and paired to CAG by age, body mass, height and gender.

The inclusion criteria for CAG were volunteers of both genders, older than 45 years with clinical diagnosis of cancer in different stages (0 to IV) and who were in treatment with chemotherapy and/or radiotherapy. For CG, volunteers of both genders, older than 45 years who were not in antidepressants and who had no chronic diseases as fibromyalgia, hypothyroidism, heart failure, chronic kidney failure, *diabetes mellitus*, pulmonary diseases and who have never been diagnosed with any type of cancer were enrolled.

CAG volunteers of both genders who presented cognitive impairment to understand how the evaluation systems were managed were excluded. In addition, individuals hospitalized, tracheostomized, with diagnosis of lung cancer or lung metastasis and who were unable to be evaluated were excluded too. The volunteers who were unable to be evaluated were excluded from the CG.

The volunteers of CAG were evaluated in the waiting room of the oncology clinic of Santa Casa of Alfenas, MG, where they were waiting for the medical consultation with the oncologist and the volunteers of the CG were evaluated in the physiotherapy clinic of UNIFAL, MG.

A pilot-study was carried out to calculate the size of the sample (G* Power software, v. 3.1.7, Franz Faul, Universität Kiel, Germany). The size N estimated for a power of 80% was 80 volunteers per group for the variable Functional Assessment of Cancer Therapy-Fatigue (FACT-F). 98 volunteers were evaluated in CAG and 86 in CG.

The height and the body mass were measured in a mechanical anthropometric balance equipped with stadiometer, both of Welmy®. The body mass index (BMI) was obtained from the values of the body mass (Kg), divided by the height squared (m^2), classified according to the World Health Organization (WHO)[25].

To determine the variables of heart and respiratory rate, the volunteers remained seated in rest. The thoracic or abdominal wall movements were observed and the number of respiratory incursions in one minute were verified to determine the respiratory rate. The heart rate was measured through the wrist in the radial artery by palpation for one minute[26].

The respiratory muscle strength was measured with manovacuometer brand *Comercial Médica* (Brazilian manufacturer, measure range 0±120mm H_2O). Variables MIP and MEP were evaluated.

After being previously instructed about the technique, the volunteer was guided to remain seated with nose clip and buccal clip in the teeth, lips tight closed to avoid air leak. To obtain MIP, forced inspiration maneuver was made from the residual volume. And, later, forced expiration from the total pulmonary capacity to obtain MEP. The procedures were repeated three consecutive times for MIP followed by MEP, with one-minute rest among the efforts and the higher value was recorded; the pressures were kept for approximately one second on verbal command[27].

Only MIP values for the analysis of the respiratory muscle weakness were considered, being ≤-70 cm H_2O acceptable strength and ≥-69 cm H_2O as non-acceptable[28], stratifying the sample in two subgroups accordingly.

The evaluation of the peripheral muscle strength was conducted with a hand dynamometer JAMAR® (Patterson Medical co. USA), with the individual seated comfortably, leaning and without support for the upper limbs. The right (RPGS) and left (LPGS) palmar grip strength was measured. The position of the upper limb for the test was kept with the shoulder adducted and neutral rotation, elbow bent at 90º, forearm in neutral position, wrist between 0° and 30° of flexion and with 0° to 15° of ulnar deviation. Three maximum voluntary contractions for each limb were requested with one-minute rest between the repetitions and considered the biggest measure obtained for each limb[29].

The questionnaire FACT-F was utilized to evaluate the fatigue and its repercussions, the instrument validated and translated into Portuguese being applicable for patients with cancer and in the general population without cancer[30].

With this questionnaire, it is possible to calculate the subscale of fatigue which addresses 13 specific items to evaluate fatigue with score from 0 to 52; as high the score, less fatigue of the individuals evaluated[30]. To determine the presence of fatigue, it was used the cutoff of 43 scores in the FACT-F subscale of fatigue. This value has sensitivity of 0.92 and specificity of 0.69 when the patients with cancer and healthy population are compared[31]. Consequently, when values below the cutoff were found, fatigue was determined.

The software Statistical Package for the Social Sciences (SPSS) (IBM Corp., Chicago, USA), version 20.0 was used for the statistical analyzes of the data.

Initially, the data were analyzed through descriptive statistical methods, being obtained the values of mean, standard deviation (SD) and confidence interval (CI 95%). Next, all the sets of the sample data were tested for normality through the Kolmogorov-Smirnov test. After this analysis, the one-way analysis of variance (Anova) test was carried out when the sample was normal. If normality was not encountered, it would be submitted to the Kruskal-Wallis test. For the categorical nominal data, the chi-square test was utilized.

In relation to the independent variables, in conformance with the criteria of normal distribution, the test *t* of Student was conducted and had these criteria have not been met, test *U* of Mann-Whitney was utilized for intergroups comparison. For both tests, the level of significance was 5%.

In addition, for all the variables, the sample power was calculated, above 0.80, it was considered high power[32]. To calculate the effect size Anova, f of Cohen was used, the values of 0.02 to 0.15 (small effect), 0.15 to 0.35 (medium effect) and above 0.35 (large effect)[32] were considered. To calculate the effect size of test *t*, the d of Cohen was utilized and adopted the values between 0.01 to 0.2 (small effect), 0.21 to 0.79 (medium effect) and equal or above 0.80 (large effect)[33]. For all the variables analyzed in this study, it was adopted level of significance of $p<0.05$.

RESULTS

Initially, 102 volunteers of the cancer group were evaluated, less four individuals with diagnosis of lung cancer, totaling the final sample of 98 volunteers. Of these, 69 underwent chemotherapy and 29, radiotherapy. For the control group, the final sample consisted of 86 individuals: 94 volunteers were evaluated, of whom, eight were excluded, two for fibromyalgia, three for hypothyroidism and three for diabetes.

The clinical and sociodemographic characteristics of the volunteers are in Table 1 and showed heterogeneity between the groups.

Table 2 presents the comparative analysis between CAG and CG for the variables of heart rate, respiratory rate, respiratory and peripheral muscle strength. It is possible to observe that the volunteers of CAG have high heart rate, reduction of the values of MEP, MIP and LPGS if compared with CG. When considering the subscale of

Table 1. Clinical and sociodemographic characteristics of the volunteers of the study

Variables		CAG (n=98) Mean (SD) (CI 95%)	CG (n=86) Mean (SD) (CI 95%)	Value of p
Age (years)*		58.13 (13.26) (55.34-60.92)	59.24 (12.87) (56.41-62.07)	0.524
BMI (kg/m2)*		26.23 (4.04) (25.87-27.65)	26.76 (4.04) (25.87-27.65)	0.336
Body mass (kg)*		67.66 (13.15) (64.89-70.44)	70.21(11.28) (67.74 -72.70)	0.162
Height (m)*		1.61 (0.09) (1.59-1.63)	1.62 (0.85) (1.60-1.64)	0.273
Gender (%)*	35.72	35.72	30.23	0.376
	64.28	64.28	69.77	
Time of diagnosis (months)		27.54 (9.61) (19.59-35.48)	-	-
Diagnostic of cancer - %(n)			-	-
Gastrointestinal tract		26.53% (26)	-	-
Breast		27.55% (27)	-	-
Abdominopelvic		28.57% (28)	-	-
Oropharynx		05.10% (05)	-	-
Others		12.25% (12)	-	-
Stages - % (n)			-	-
0		26.54% (26)	-	-
I		8.16% (08)	-	-
II		29.59 (29)	-	-
III		25.51 (25)	-	-
IV		10.20 (10)	-	-
Types of treatment % (n)#			-	
Chemotherapy		(70.40) 69	-	
Chemotherapy/Radiotherapy		(29.60) 29	-	
Presence of fatigue - %(n)#				
Yes		67.35 (62)	33.72 (29)	0.009
No		32.65 (36)	66.28 (57)	0.029
CRMS % (n)#				
Acceptable		42.88 (42)	79.06 (68)	0.013
Non-acceptable		57.12 (56)	20.94 (18)	<0.001

Captions: SD: standard deviation; CI: confidence interval; BMI: body mass index; M: male; F: female; CRMS: classification of respiratory muscle strength. Others: (leukemia, lymphoma, bone cancer, brain cancer and skin cancer).
Note: *test Anova; # χ^2: chi-square test.

fatigue, it was noticed that the volunteers of CAG were significantly fatigued in comparison with CG (cutoff of the subscale of fatigue = 43 scores).

The analyzes of the variables of the CAG and CG according to the subgroups of acceptable and non-acceptable respiratory muscle strength are presented in Tables 3 and 4.

While analyzing the respiratory variables and of the PGS (palmar grip strength) of the volunteers of CAG by the classification of the acceptable and non-acceptable muscle respiratory strength, lower values were observed for the volunteers of non-acceptable respiratory muscle strength in relation to the variables MEP, MIP, RPGS, LPGS than the volunteers of acceptable strength. The number of volunteers of CAG who presented non-acceptable strength is 21.81% bigger than those who presented acceptable strength. There is no difference among the volunteers of CAG who have acceptable and non-acceptable muscle respiratory strength in relation to the subscale of fatigue (Table 3).

When analyzing the respiratory variables and of PGS of the volunteers of CG who present acceptable or non-acceptable respiratory muscle strength, lower values for the volunteers of non-acceptable strength in relation to variables MEP, MIP, RPGS, LPGS were observed than in the volunteers of acceptable strength. The number of volunteers of CG who present non-acceptable strength is 73.52% lower than those who present acceptable strength. There is difference between the volunteers of the CG who have acceptable and non-acceptable respiratory muscle strength in relation to the subscale of fatigue (Table 4).

DISCUSSION

Antineoplastic treatment is fundamental for the several types of cancer, which results in improvement of quality of life. However, it offers potential risks of toxicity for causing side effects as cardiovascular alterations[23,34,35].

A significant increase of the heart rate in CAG in comparison with CG was noticed. It is believed that this change may have been chemotherapy induced, although the types of chemotherapics and its action were not object of investigation in the present study. These drugs can weaken the heart muscle (cardiomyopathy) and induce disorders as supraventricular and ventricular arrythmias[34,35], in addition to damaging the respiratory system[10,12,18].

Respiratory muscle strength can be compromised in patients with cancer treated with chemotherapy[17,36]. This fact justifies the investigation of the maximum respiratory pressures[36], because the reduction of its values demonstrates the presence of muscle weakness[35] and could relate to fatigue reported by the subjects[37]. In the present study, chemotherapy and/or radiotherapy

Table 2. Comparative analysis of the heart rate, respiratory rate, subscale of fatigue and peripheral and respiratory muscle strength of the cancer and control groups

Variables	CAG (n=98) Mean (SD) (CI 95%)	CG (n=86) Mean (SD) (CI 95%)	Value of p	f^2
HR (bpm)	77.11 (12.68) (74.44-79.78)	71.17 (11.28) (68.69-73.64)	0.002*	0.162
RR (ripm)	17.04 (4.27) (16.14-17.94)	17.86 (4.04) (16.97-18.75)	0.086	0.098
MEP (cm/H_2O)	75.54 (28.86) (69.46-81.62)	94.88 (24.57) (89.48-100.28)	<0.001*	0.361
MIP (cm/H_2O)	-67.71 (32.60) (60.84-74.57)	-93.31 (25.25) (87.77-98.86)	<0.001*	0.441
RPGS (kgf)	23.60 (10.24) (21.44-25.76)	26.13 (9.85) (23.97-28.29)	0.110	0.126
LPGS (kgf)	21.48 (9.51) (19.48-23.48)	24.89 (9.19) (22.87-26.91)	0.024*	0.182
Subscale of fatigue	37.14 (10.57) (34.91-39.37)	44.24 (7.96) (42.49-45.98)	<0.001*	0.382

Captions: SD: standard deviation; CI: confidence interval; CAG: cancer group; CG: control group; HR: heart rate; RR: respiratory rate; MEP: maximum expiratory rate; MIP: maximum inspiratory rate; RPGS: right palmar grip strength; LPGS: left palmar grip strength.
Note: *p<0.05, test of Kruskal-Wallis; f of Cohen: effect size.

Table 3. Comparative analysis of the subscale of fatigue and variables of respiratory and peripheral hand grip strength of the volunteers of the cancer group who presented fatigue (non-acceptable) or not (acceptable) of the respiratory muscle

Variables	Acceptable (n=43) Mean (SD) (CI 95%)	Non-acceptable (n=55) Mean (SD) (CI 95%)	Value of p	d
MEP (cm/H_2O)	97.39 (18.42) (91.34-103.45)	64.47 (20.99) (57.93-71.02)	<0.001*	1.667
MIP (cm/H_2O)	100.68 (15.71) (95.52-105.85)	48.14 (14.48) (43.63-52.65)	<0.001*	3.478
RPGS (kgf)	27.46 (11.02) (23.84-31.08)	21.74 (9.26) (18.85-24.62)	0.005*	0.562
LPGS (kgf)	25.21 (10.05) (21.91-28.51)	19.36 (9.15) (16.50-22.21)	<0.001*	0.609
Subscale of fatigue	36.82 (11.84) (32.92-40.71)	37.32 (10.33) (34.10-40.54)	0.960	0.045

Captions: SD: standard deviation; CI: confidence interval; MEP: maximum expiratory pressure; MIP: maximum inspiratory pressure; RPGS: right palmar grip strength; LPGS: left palmar grip strength.
Note: *p<0.05, Mann-Whitney test; d of Cohen: effect size. .

Table 4. Comparative analysis of the subscale of fatigue of variables of respiratory and peripheral muscular strength of the volunteers of the control group who presented fatigue (non-acceptable) or not (acceptable) of the respiratory muscle

Variables	Acceptable (n=68) Mean (SD) (CI 95%)	Non-acceptable (n=18) Mean (SD) (CI 95%)	Value of p	d
MEP (cm/H_2O)	99.91 (22.02) (94.54-105.28)	75.65 (24.04) (63.28-88.01)	<0.001*	1.052
MIP (cm/H_2O)	102.81 (17.82) (98.46-107.15)	54.12 (10.87) (48.53-59.71)	<0.001*	3.299
RPGS (kgf)	27.57 (10.13) (25.09-30.04)	20.00 (5.02) (17.41-22.58)	0.002*	0.947
LPGS (kgf)	26.13 (9.42) (23.83-28.43)	19.65 (5.89) (16.61-22.68)	0.003*	0.825
Subscale of fatigue	44.75 (8.01) (42.80-46.71)	42.17 (7.11) (38.52-45.83)	0.037*	0.341

Captions: SD: standard deviation; CI: confidence interval; MEP: maximum expiratory pressure; MIP: maximum inspiratory pressure; RPGS: right palmar grip strength; LPGS: left palmar grip strength.
Note: *p<0.05, Mann-Whitney test; d of Cohen: effect size.

promoted the reduction of the inspiratory and expiratory muscle strength. This weakness could be associated to modifications of the pulmonary parenchyma, in addition to fatigue and physical exhaustion caused by the antineoplastic treatment[12,17,38].

In another study, when comparing patients with cancer and patients with other diseases, it was noticed reduction of the pulmonary function and of the peripheral muscle strength[18]. These data corroborate the findings of the present study.

The PGS is a general indicator of peripheral muscle strength and power and is related to rates of morbidity and mortality[8,18]. In addition, this variable associates with cardiovascular diseases and cancer[39], and its decline demonstrates the reduction of autonomy to perform daily life activities[23]. Chemotherapy and/or radiotherapy reduced the palmar grip strength for both limbs evaluated, but this was not significant for the right limb. It is possible that the concentration of volunteers with breast cancer with the left limb affected (n=19, data not evaluated) may have influenced the findings. Another consideration that may have influenced the result was that for both groups, these values were lower than of the Brazilian populational reference[40].

The effects of CRF are multidimensional and can interfere in all aspects of the life of an individual, including independence, muscle strength, concentration and social relations and be extremely anguishing[5,13].

The volunteers in chemotherapy and/or radiotherapy treatment changed the medium level of CRF. It has been reported that cancer survivors experienced a significant increase of the fatigue after chemotherapy, radiotherapy and/or biological therapies[41]. In addition, this treatment can reduce the peripheral and respiratory muscle strength and few studies on that matter were detected[18,42].

Whether or not respiratory weakness is present, CRF keeps high during chemotherapy and/or radiotherapy. The symptom of fatigue is related to the cancer itself and treatment side effects, among which toxicity to chemotherapy[20] and to radiotherapy[41], which is not different from the present study findings. In 2018, Morishita et al.[43] also reported more fatigue in volunteers with cancer when compared to healthy individuals but association with peripheral muscle strength was not found.

The volunteers without cancer who presented respiratory muscle weakness also reduced the PGS and presented fatigue. The PGS holds association with pulmonary function in young and healthy adults[44] and in older adults[45], like the findings of the present study where, as big the peripheral muscle strength, greater is the respiratory strength.

CONCLUSION

The study demonstrated that the volunteers with cancer in chemotherapy and/or radiotherapy had reported fatigue and reduction of the peripheral and respiratory muscle strength in comparison with volunteers without cancer. When groups were stratified regarding muscle strength, volunteers with and without cancer had the same peripheral respiratory and muscle behavior but healthy individuals with respiratory muscle weakness can report fatigue.

The study had not the objective of correlating the variables to the types of cancer and stages. In addition, the chemotherapics types were not specified in cancer treatment and its relations with the study variables. The study did not analyze the scale FACT-F, which can signify a new angle about quality of life of individuals with cancer and its connection with the respiratory variables investigated.

CONTRIBUTIONS

Karina Oliveira Prado Mariano, Ricardo da Silva Alves, Carmélia Bomfim Jacó Rocha, Denise Hollanda Iunes, Juliana Bassalobre Carvalho Borges and Leonardo Cesar Carvalho contributed for the conception and/or design of the study; collection, analysis and interpretation of the data, wording and critical review Ana Paula Aparecida Mantuani and Sabrina Rosse Carvalho contributed for the conception and/or design of the study, collection, analysis and interpretation of the data. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

Coordination for the improvement of higher education personnel (CAPES), Brazil – Code 001; Post-graduation program in Sciences of Rehabilitation of UNIFAL, MG and Tutorial Education Program (PET-MEC-SESU).

REFERENCES

1.
2. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi: https://doi.org/10.3322/caac.21492
3. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91. doi: https://doi.org/10.1136/gutjnl-2015-310912
4. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020 : incidência de Câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2019 [acesso 2020 jun 28]. Available from: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2020-incidencia-de-cancer-no-brasil.pdf
5. Ryan JL, Carroll JK, Ryan EP, et al. Mechanisms of cancer-related fatigue. Oncologist. 2007;12(Suppl 1):22-34. doi: https://doi.org/10.1634/theoncologist.12-S1-22
6. Berger AM, Mooney K, Alvarez-Perez A, et al. Cancer-Related Fatigue, Version 2.2015. J Natl Compr Canc Netw. 2015;13(8):1012-39. doi: https://doi.org/10.6004/jnccn.2015.0122
7. Humphreys J, de la Maza P, Hirsch S, Barrera G, Gattas V, Bunout D. Muscle strength as a predictor of loss of functional status in hospitalized patients. Nutrition. 2002;18(7-8):616-20. doi: https://doi.org/10.1016/s0899-9007(02)00756-6
8. Novaes RD, Miranda AS, Silva JO, et al. Equações de referência para a predição da força de preensão manual em brasileiros de meia idade e idosos. Fisioter Pesqui. 2009;16(3):217-22. doi: https://doi.org/10.1590/S1809-29502009000300005

9. Chung CJ, Wu C, Jones M, et al. Reduced handgrip strength as a marker of frailty predicts clinical outcomes in patients with heart failure undergoing ventricular assist device placement. J Card Fail. 2014;20(5):310-5. doi: https://doi.org/10.1016/j.cardfail.2014.02.008
10. Spruit MA, Sillen MJH, Groenen MTJ, et al. New normative values for handgrip strength: results from the UK Biobank. J Am Med Dir Assoc. 2013;14(10):775.e5-11. doi: https://doi.org/10.1016/j.jamda.2013.06.013
11. Baldwin CE, Bersten AD. Alterations in respiratory and limb muscle strength and size in patients with sepsis who are mechanically ventilated. Phys Ther. 2014;94(1):68-82. doi: https://doi.org/10.2522/ptj.20130048
12. Sawada NO, Nicolussi AC, Okino L, et al. Avaliação da qualidade de vida de pacientes com câncer submetidos à quimioterapia. Rev Esc Enferm USP. 2009;43(3):581-7. doi: https://doi.org/10.1590/S0080-62342009000300012
13. Spyropoulou D, Leotsinidis M, Tsiamita M, et al. Pulmonary function testing in women with breast cancer treated with radiotherapy and chemotherapy. In Vivo. 2009;23(5):867-71.
14. Savina S, Zaydiner B. Cancer-related fatigue: some clinical aspects. Asia Pac J Oncol Nurs. 2019;6(1):7-9. doi: https://doi.org/10.4103/APJON.APJON_45_18
15. da Silva Alves R, Iunes DH, Pereira IC, et al. Influence of exergaming on the perception of cancer-related fatigue. Games Health J. 2017;6(2):119-26. doi: https://doi.org/10.1089/g4h.2016.0051
16. Oliveira PF, Iunes DH, Alves RS, et al. Effects of exergaming in cancer related fatigue in the quality of life and electromyography of the middle deltoid of people with cancer in treatment: a controlled trial. Asian Pac J Cancer Prev. 2018;19(9):2591-7. doi: https://doi.org/10.22034/APJCP.2018.19.9.2591
17. Abreu APM, Endres D, Costa AB, et al. Função pulmonar e força muscular respiratória em pacientes submetidas à cirurgia oncológica de mama. Rev Bras Cancerol. 2014;60(2):151-7. doi: https://doi.org/10.32635/2176-9745.RBC.2014v60n2.484
18. Schettino RC, Jotta LMGN, Cassali GD. Função pulmonar em mulheres com câncer de mama submetidas à radioterapia: um estudo piloto. Fisioter Pesqui. 2010;17(3):248-52. doi: https://doi.org/10.1590/S1809-29502010000300011
19. Celis-Morales CA, Welsh P, Lyall DM, et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. BMJ. 2018;361:K1651. doi: https://doi.org/10.1136/BMJ.K1651
20. Servaes P, Verhagen C, Bleijenberg G. Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. Eur J Cancer. 2002;38(1):27-43. doi: https://doi.org/10.1016/s0959-8049(01)00332-x
21. Waseem M, Kaushik P, Tabassum H, et al. Role of Mitochondrial Mechanism in Chemotherapy-Induced Peripheral Neuropathy. Curr Drug Metab. 2018;19(1):47-54. doi: https://doi.org/10.2174/1389200219666171207121313
22. Suesada MM, Carvalho HA, Albuquerque ALP, et al. Impact of thoracic radiotherapy on respiratory function and exercise capacity in patients with breast cancer. J Bras Pneumol. 2018;44(6):469-76. doi: https://doi.org/10.1590/S1806-37562017000000120
23. American Thoracic Society; European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002;166(4):518-624. doi: https://doi.org/10.1164/rccm.166.4.518
24. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc. 2019;51(11):2375-90. doi: https://doi.org/10.1249/MSS.0000000000002116
25. Prinsen H, van Dijk JP, Zwarts MJ, et al. The role of central and peripheral muscle fatigue in postcancer fatigue: a randomized controlled trial. J Pain Symptom Manage. 2015;49(2):173-82. doi: https://doi.org/10.1016/j.jpainsymman.2014.06.020
26. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157-63. doi: https://doi.org/10.1016/S0140-6736(03)15268-3
27. Porto CC. Semiologia Médica. 8. ed. Rio de Janeiro: Guanabara Koogan; 2019.
28. Koulouris N, Mulvey DA, Laroche CM, et al. Comparison of two different mouthpieces for the measurement of Pimax and Pemax in normal and weak subjects. Eur Respir J. 1988;1(9):863-7.
29. Azeredo CAC. Fisioterapia respiratória moderna. São Paulo: Manole; 2002.
30. Ashton L, Myers S. Serial grip strength testing- its role in assessment of wrist and hand disability. Internet J Surg. 2003;5(2).
31. Ishikawa NM, Thuler LCS, Giglio AG, et al. Validation of the portuguese version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian cancer patients. Support Care Cancer. 2010;18(4):481-90. doi: https://doi.org/10.1007/s00520-009-0697-0
32. Cella D, Lai JS, Chang CH, et al. Fatigue in cancer patients compared with fatigue in the general United States population. Cancer. 2002;94(2):528-38. doi: https://doi.org/10.1002/cncr.10245
33. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. New Jersey: Lawrence Erlbaum; 1988. doi: https://doi.org/10.4324/9780203771587

34. Lindenau JDR, Gimarães LSP. Calculando o tamanho de efeito no SPSS. Rev HCPA. 2012;32(3):363-81.
35. Dolci A, Dominici R, Cardinale D, et al. Biochemical markers for prediction of chemotherapy-induced cardiotoxicity: systematic review of the literature and recommendations for use. Am J Clin Pathol. 2008;130(5):688-95. doi: https://doi.org/10.1309/AJCPB66LRIIVMQDR
36. Suter TM, Ewer MS. Cancer drugs and the heart: Importance and management. Eur Heart J. 2013;34(15):1102-11. doi: https://doi.org/10.1093/eurheartj/ehs181
37. Coelho CM, Carvalho RM, Gouvêa DSA, et al. Comparação entre parâmetros de pressões respiratórias máximas em indivíduos saudáveis. J Bras Pneumol. 2012;38(5):605-13. doi: https://doi.org/10.1590/S1806-37132012000500010
38. Santos DE, Rett MT, Mendonça ACR, et al. Efeito da radioterapia na função pulmonar e na fadiga de mulheres em tratamento para o câncer de mama. Fisioter Pesqui. 2013;20(1):50-5. doi: https://doi.org/10.1590/S1809-29502013000100009
39. Reidunsdatter RJ, Rannestad T, Frengen J, et al. Early effects of contemporary breast radiation on health-related quality of life - Predictors of radiotherapy-related fatigue. Acta Oncol. 2011;50(8):1175-82. doi: https://doi.org/10.3109/0284186X.2011.604345
40. Ruiz JR, Sui X, Lobelo F, et al. Association between muscular strength and mortality in men: prospective cohort study. BMJ. 2008;337(7661):a439. doi: https://doi.org/10.1136/bmj.a439
41. Caporrino FA, Faloppa F, Santos JBG, et al. Estudo populacional da força de preensão palmar com dinamômetro Jamar ®. Rev Bras Ortop. 1998;33(2):1-1.
42. Ebede CC, Jang Y, Escalante CP. Cancer-related fatigue in cancer survivorship. Med Clin North Am. 2017;101(6):1085-97. doi: https://doi.org/10.1016/j.mcna.2017.06.007
43. Steemburgo T, Averbuch NC, Belin CHS, et al. Hand grip strength and nutritional status in hospitalized oncological patients. Rev Nutr. 2018;31(5):489-99. doi: https://doi.org/10.1590/1678-98652018000500006
44. Morishita S, Tsubaki A, Fu JB, et al. Cancer survivors exhibit a different relationship between muscle strength and health-related quality of life/fatigue compared to healthy subjects. Eur J Cancer Care (Engl). 2018;27(4):e12856. doi: https://doi.org/10.1111/ECC.12856
45. Mgbemena NC, Aweto HA, Tella BA, et al. Prediction of lung function using handgrip strength in healthy young adults. Physiol Rep. 2019;7(1):e13960. doi: https://doi.org/10.14814/phy2.13960
46. Bahat G, Tufan A, Ozkaya H, et al. Relation between hand grip strength, respiratory muscle strength and spirometric measures in male nursing home residents. Aging Male. 2014;17(3):136-40. doi: https://doi.org/10.3109/13685538.2014.936001

Recebido em 20/5/2020
Aprovado em 9/7/2020