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Study of the Effect of Exercises on the Quality of Life, Fatigue, Sarcopenia in Breast, and Prostate and Colorectal Cancers

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Abstract: Breast, prostate, and colorectal cancers are the most common cancers and have the highest mortality rates worldwide. *Objective:* To determine the benefits of continuous training at moderate and high intensity on quality of life, fatigue and sarcopenia in breast, prostate, and colorectal cancer. *Method:* A quasi-experimental study was performed with 356 patients with stage II breast cancer. The patients were distributed in 2 groups, and EORTC QLQ C-30 scale, FACT- Fatigue Scale, quality of life test, stress test, dynamometry and others were carried out. *Results:* The study population presented with sarcopenia. At the end of the study, the prevalence of sarcopenia decreased significantly (GE1: 31 % [before] vs. 24 % [after], and GE2: 38 % [before] vs. 19 % [after]; $P \leq 0.05$). As did the values for fatigue (GE1: 17.3 ± 3.8 [before] vs. 10.4 ± 2.5 [after], and GE2: 19.6 ± 4.2 [before] vs. 9.4 ± 3.1 [after]; $P = 0.012$) and in the quality-of-life questionnaire (GE1: 61.7 ± 10.4 [before] vs. 69.5 ± 14.4 [after]; GE2: 76.5 ± 7.4 [before] vs. 106; $P = 0.005$). *Conclusion:* Continuous training at moderate and high intensity inevitably improved the variables evaluated, especially quality of life, fatigue, and sarcopenia. It should be noted that the improvements were more notable in the high intensity group.

Keywords: Cancer; Aerobic exercise; High intensity training; Strength training

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1. Introduction

Cancer is considered a systemic disease worldwide, which causes morbidity and mortality by affecting organs and tissues. More than 14 million people are diagnosed with cancer worldwide and 8 million die from it each year. The most common types of cancer are lung, breast, prostate, and colorectal cancers. Cancers are associated with various factors: genetics, age (> 40 years), sex (male: higher prevalence), race (< 40 years: white; > 40 years: African-American/black), lifestyle, environmental factors, and also human papillomavirus (HPV), human immunodeficiency virus (HIV), and Epstein-Barr virus (EBV) [1]. Malignant tumors are also formed, although other factors play a role in their development, such as hormones, tobacco and alcohol consumption, psychological stress, diet [2], and increased exposure to carcinogens [3].

Quality-of-life assessment depends on the progress of disease and treatment, optimistic attitudes, autonomy and rights, as well as psychosocial aspects, in addition to constant demographic and epidemiological evolution [3,4].

Breast cancer is a neoplasm that requires intense and continuous treatment, with physical, physiological, mental, and psychosocial effects, negatively affecting the patient's quality of life. Likewise, the decrease muscle mass, i.e., sarcopenia, leads to fatigue (78%–96% of people), somnolence, anxiety, stress, myocardial, coronary, carotid, and ventricular alterations, which decrease ejection fraction [5,6].

However, colorectal cancer is the second leading cause of death worldwide and the fifth most common malignant tumor, with a higher incidence in developing countries than in developed countries, with Japan, China and Korea accounting for 60% of cases [7]. Besides, prostate cancer is the second leading cause of death and the most common cause of death in Chile and the USA [8]. Pharmacological treatments for cancers the affect quality of life, endocrine system, and causes fatigue, muscle weakness, discouragement, limited sexual and cognitive desire and function, increased insulin resistance, anemia, and dyslipidemia; all this together with psychosocial problems [9] and many other alterations [10].

However, according to literature, physical exercises reduce adverse effects, and a change in eating habits helps to improve quality of life and reduce anxiety and fear of relapse [11]. In addition, it will improve the physical condition, weight, and muscle mass of the patient. Moreover, several studies have shown that high intensity interval training (HIIT) and moderate intensity interval training (MICT) are useful for increasing cardio-respiratory capacity, mitochondrial, muscle biogenesis, GLUT-4, HbA1c, and others [12-14]. Therefore, the aim of this research is to determine the benefits of MICT and HIIT on quality of life, fatigue, and sarcopenia in breast, prostate and colorectal cancer patients.

2. Methodology

A quasi-experimental descriptive study combined with analysis of quantitative variables was conducted in the city of Cúcuta, Colombia, with an initial sample of 1,573 patients within a period of 3 years and 4 months. After the different filtering, this research was conducted with 356 patients with stage II breast, prostate, or colorectal cancers. The patients were divided into 2 groups (MICT and HIIT) using basic probability sampling, which was a table of numbers, in which the order of patients was randomized through Excel. As a result, experimental group 1 (GE1) consisted of 177 participants and experimental group 2 (GE2) consisted of 179. It should be noted that this article is part of the ONCO-EXE TRIAL macro-project registered in ClinicalTrials.gov NCT03915288 (**Figure 1**).

2.1. Characteristics of participants

The participants of this study are similar in terms of cancer stage, ejection fraction, functional class, muscle percentage, fat and body mass index, abdominal circumference, prevalence of diabetes, and hypertension, and they are classified as "high risk" in terms of cardiovascular risk according to the American Association for Cardiopulmonary Rehabilitation stratification [15].

2.2. Inclusion criteria

Participants with stage II cancer, over 18 years of age, and who are willing to participate in the program. They signed an informed consent form and were protected by the Ethics and Research Committee of the CEI-FISICOL institution. They were also required to present a mandatory ejection fraction of 35% and above, without any impediment to present the tests, surveys, and research.

2.3. Exclusion criteria

Participants were excluded if they reported severe lower limb pain, heart rate instability or >120 bpm at rest, angina, systolic blood pressure > 190mmHg, diastolic > 120mmHg, and participants that are not of stage II cancer were excluded. Besides, the individual had the choice to leave the investigation at any time or upon showing hemodynamic instability without improvement.

2.4. The blind method

At the beginning, assessments were carried out by an external medical oncologist. Subsequently, the information was entered into the database at Microsoft Excel using a number for identification, and then randomization was carried out by an engineer from the institution and an external engineer.

The researchers carried out the forms and tests without any information about the participants or the type of cancer they had, or their intervention group. Only the lead author held periodic meetings with the physiotherapist trainers to understand training of the participants without any knowledge of the data. At the end of the program, the participants were evaluated again for quantification, comparison, and statistical analysis, in a blinded manner by the authors. After the different variables were studied, all authors were notified to generate conclusions together.

2.5. Anthropometric characteristics

The participants' personal and family history was obtained using a separate form, as well as anthropometric measurements (weight, height, body mass index (BMI), and abdominal circumference), and the percentage of muscle and adipose tissue.

To obtain the weight and the percentage of adipose and muscle tissue, a calibrated TezzioTB-30037 digital scale was used. The Adult Acrylic Halter Wall Kramer 2104 was used to obtain the height, where the participant stood in a bipedal position, facing forward, with upper limbs relaxed and close to the body, with an upright back resting on a flat surface to avoid lordosis with the feet. With these values, the BMI was determined. Subsequently, the abdominal circumference was measured using a measuring tape, while taking into account the anatomical values described by Frisancho [16].

2.6. Clinical and hemodynamic parameters

Each participant underwent 2-D echocardiography at baseline and at the end of the program to identify the structures involved, left ventricular ejection fraction (LVEF), and to analyze mobility in real time. In addition, physical function was assessed individually according to the New York Heart Association (NYHA) classification; and dyspnea and fatigue was assessed according to the modified Borg scale [17]. The patients' heart rates were measured using the Polar Multisport RS800CX system, and their respiratory rate and blood pressure were obtained manually and corroborated by a second evaluator, while a Nellcor Puritan Bennett® oximeter was used to obtain oxygen saturation.

2.7. Questionnaires, tests, and quizzes

At the beginning, the participants had to undergo an assessment by the medical oncology department which included the current status, anthropometric, and physical measurements of the participant. At the same time, the participants' exercise tolerance were also evaluated by a physiotherapist according to the ATS Statement: Guidelines for the six-minute-walk test of the American Thoracic Society [18,19].

The following day, participants returned for the Naughton stress test with prior advice not to drink stimulant beverages, smoke and/or ingest drugs or substances that would alter consciousness or vital signs.

2.8. Sarcopenia

We used the European Consensus on Sarcopenia (2010) [20], which was based on three criteria: gait examination, muscle strength, and muscle mass. For the first criterion, we used the Short Physical Performance Battery (SPPB) modified by Guralnik *et al.* [21]. For the second criterion, the participants' muscle strength was measured. As for the last criterion, muscle mass was assessed based on BMI and calf circumference (cut-off point 31cm) [20].

2.9. Strength

It was assessed by dynamometry with Hand Grip CAMRY Electronic hand dynamometer model EH101 where the participants were seated without support on the forearms, arms held laterally against the body alignment. Their elbows were flexed to a 90° angle, while their forearm and wrist remain in a neutral position. The assessment was performed on the dominant side with 3 repetitions and 1 min rest, as well as the non-dominant side. For maximal strength, a test of one repetition maximum (1RM) was performed.

2.10. Quality of life

The EORTC QLQ C-30 questionnaire [22] was used with appropriate modifications [23]. This test was requested from the EORTC Quality of Life Group website who approved its use in this study.

2.11. Fatigue

Fatigue was assessed using the FACT-Fatigue Scale (Functional Assessment of Cancer Laterapy Fatigue Scale), which is a 13-item scale that assesses the severity of cancer-associated fatigue (FAC) in the past week [24].

2.12. Interventions

The training program was set according to the FCM obtained in the stress test and strength test, and the result of the 1RM test was also considered. The training program lasted 36 weeks, 3 sessions a week, and 70 min per session. Patients were monitored by the Polar Multisport RS800CX system, oximetry, and the Borg scale. The incline, resistance, or speed of the exercises were assigned according to the indicative parameters (FCM, VO_2, Borg) for moderate and high intensity exercises.

2.13. Experimental group 1 (*n* = 177)

The 70 min sessions included a 10 min warm-up (breathing exercises, walking, and stretching), 30 min of continuous aerobic training at moderate intensity (60-80 % FCM) like cycling, rowing machine, elliptical, and recumbent. The other 20 min were for strength training (40-60 % maximal strength), and the last 10 min were for cool down (coordination exercises, balance, walking, and breathing exercises).

2.14. Experimental group 2 (*n* = 179)

The warm-up, strength training, and cool-down were identical to GE1. The following 30 min were HIIT intervallic exercise with a protocol created by the main author which we call 30-30. 30sec at moderate intensity (60-80% FCM) and 30sec at high intensity (80-90% FCM) on a treadmill, exercise bike, rowing, and recumbent.

2.15. Statistical analysis

A database was created in Microsoft Excel and descriptive statistical analysis was then performed to evaluate the data based on average values and their corresponding standard deviation. The normality of the data was assessed using the Kolmogorov-Smirnov test, and the indication of specificity was evident for all analyses. Furthermore, Tukey's test and analysis of variance ANOVA (two-way analysis of variance) were carried out followed by post hoc tests. In all cases, a significance level of 5 % ($P < 0.05$) was established and everything was carried out in the accordingly.

2.16. Ethical considerations

This study was designed and developed under the ethical considerations of the Helsinki Declaration, which involved signing of an informed consent by the patients, and an approval from the managers, coordinators, and ethics committee of the institution.

3. Result

After filtering, 356 patients in 2 groups (GE1 and GE2) with stage II breast (GE1-45 % and GE2-39 %), prostate (GE1-43 % and GE2-46 %) and colorectal (GE1-12 % and GE2-15 %) cancers were included in this study.

Regarding the academic level of the participants, 43.8 % (*n* = 156) had only completed primary school, 23.5 % (*n* = 84) studied up to secondary school, 19.3 % (*n* = 69) university level, and 13.2 % (*n* = 47) have not received formal education. The oncological treatments performed were surgery (26%), radiotherapy (62%), chemotherapy (47%), and hormone therapy (43%). The most prevalent risk factors in the study population were sedentary lifestyle, obesity, malnutrition, smoking, and many others (**Table 1**).

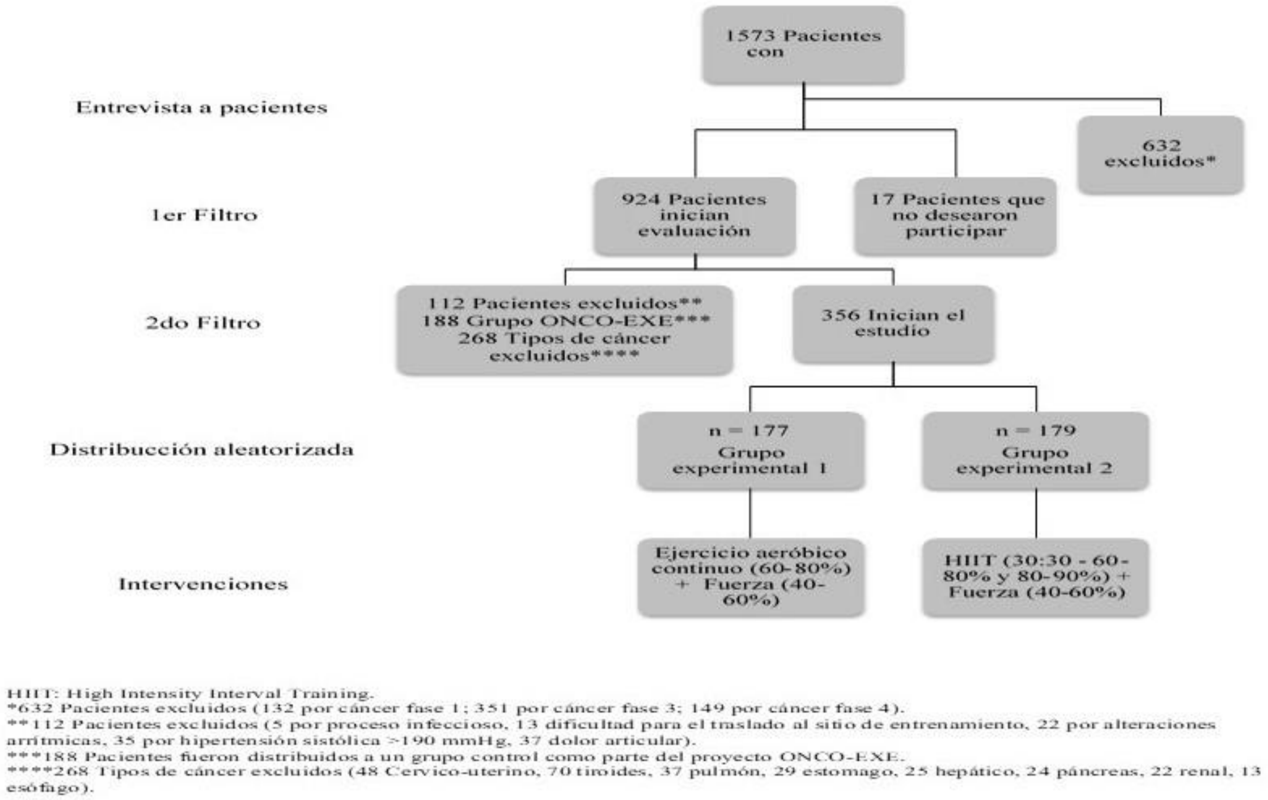
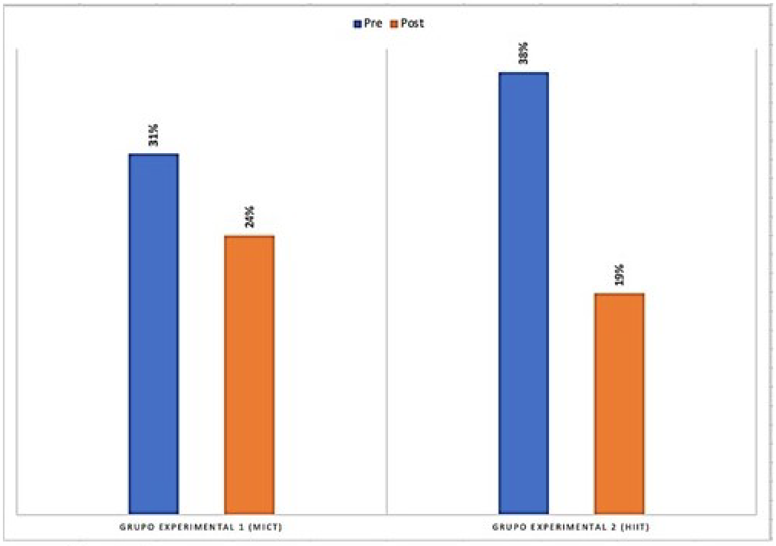


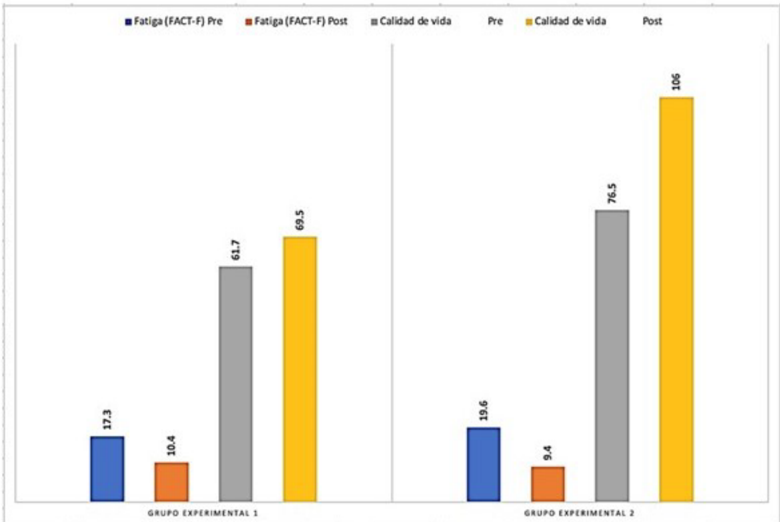
Figure 1. Flow chart of the distribution (*n* = 1573)

A significant percentage of the study population were diagnosed with sarcopenia based on the aforementioned criteria. After the training program, the prevalence of sacropenia decreased significantly, with GE2 showing greater impact (GE1: 31 % [before] vs. 24 % [after], and GE2: 38 % [before] vs. 19 % [after]; $P \leq 0.05$), as shown in **Figure 2**. As for the values for cancer-associated fatigue (GE1: 17.3 [before] ± 3.8 vs. 10.4 ± 2.5 [after] and GE2: 19.6 ± 4.2 [before] vs. 9.4 ± 3.1 [after]; *P* = 0.012) and in the EORTC QLQC-30 questionnaire for quality of life (GE1: 61.7 ± 10.4 [before] vs. 69.5 ± 14.4 [after]; GE2: 76.5 ± 7.4 [before] vs. 106 [after]; *P* = 0.005), as shown in **Figure 3**.



	Pre	Post
Grupo experimental 1 (MICT)	31 %	24 %
Grupo experimental 2 (HIIT)	38 %	19 %

Figure 2. Prevalence of sarcopenia pre- and post-training



	Fatiga (FACT-F) Pre	Fatiga (FACT-F) Post	Calidad de vida Pre	Calidad de vida Post
Grupo Experimental 1	17,3	10.4	61,7	69,5
Grupo Experimental 2	19,6	9.4	76,5	106

Figure 3. Fatigue and quality of life associated with post-training cancer

In terms of hemodynamic variables after the training program, we were able to determine changes in ejection fraction (GE1: 48 ± 2.7 [before] vs. 50 ± 3.2 [after]; GE2: 49 ± 1.8 [before] vs. 54 ± 2.6 [after]; $P = 0.003$) and maximum heart rate (GE1: 150±4.6 vs. 152 ± 8; GE2: 152 ± 3.5 vs. 155 ± 7; P = 0.012) (**Table 2**). Also, it is worth mentioning that no complications or adverse events occurred during the training program. Furthermore, it is noteworthy that during the training sessions, participants reported a perceived dyspnea according to the Borg scale between 6 and 8 (moderate intensity) in groups 1 and 2, with group 2 reporting peaks between 9 and 10, as well as feelings of peri-exercise fatigue.

Table 1. Baseline characteristics of participants (n = 356)

Cuadro 1. Caracteristicas iniciales de los participantes (n= 356).

Características	GE 1 n= 177	GE 2 n= 179
Cáncer próstata	76 (42,9 %)	82 (45,8 %)
Cáncer mama	80 (45,1 %)	70 (39,1 %)
Cáncer Colorrectal	21 (11,8 %)	27 (15 %)
Sexo	H: 87 M: 90	H: 94 M: 85
Edad (Años)	54 ± 5	56 ± 4
Fracción de eyección (%)	48 ± 2,7	49 ± 1,8
Altura (m)	1,54 ± 7,1	1,60 ± 9,3
Peso (kg)	80 ± 12,7	82 ± 9,7
IMC	33,7 ± 3,9	32 ± 3,1
Circunferencia abdominal (cm)	89 ± 5,5	85 ± 6,7
Porcentaje graso (%)	19 ± 4,4	17 ± 3,8
Porcentaje muscular (%)	25 ± 5,1	23 ± 2,3
Fuerza	30,3 ± 2,7	28 ± 3,6
Sarcopenia (%)	31 %	38 %
Circunferencia pantorrilla	32 ± 9,3	31,3 ± 5,6
Vo2 estimado	13,2 ± 5,2	11,5 ± 4,7
Fatiga (FACT-F)	17,3 ± 3,8	19,6 ± 4,2
Calidad de vida	61,7 ± 10,4	76,5 ± 7,4
Distancia recorrida	363 ± 25	332 ± 20
FCM en prueba de esfuerzo	150 ± 4,6	152 ± 3,5
Sobrepeso y/u obesidad	72 %	79 %
Obesidad abdominal	51 %	58 %
Dislipidemia	25 %	30 %
Hipertensión arterial	31 %	40 %
Diabetes	12 %	17 %
Enfermedad renal	8 %	10 %
Sedentarismo*	92 %	93 %
Depresión	51 %	56 %
Ansiedad	18 %	21 %
Tabaquismo	35 %	40 %
Alcoholismo	11 %	16 %
Ingesta de comida inadecuada	40 %	51 %
Historial de IMC	3 %	4 %
Sexo femenino	51 %	47 %
Edad †	4 %	5 %

IMC: indice de masa corporal; VO2: consumo máximo de oxigeno; FCM: frecuencia cardiaca máxima; kilogramos; %: porcentaje; cm: centimetros; m: metros. IAM: infarto agudo de miocardio.
* Menos de 150 min por semana.
† Mujer > 65 años y Hombres > 40 años según *Rev Colomb Cardiol. 2011;18(4):177-182.*

Table 2. Post-training change analysis (n = 356)

	GE 1 n= 177		GE 2 n= 179		G1 Vs G2
Variables	Pre	Pos	Pre	Pos	Valor *P*
Fracción de eyección (%)	48±2,7	50±3,2	49±1,8	54±2,6	0,003
Peso (kg)	80±12,7	76±4,1	82±9,7	75±3,5	0,001
Índice de masa corporal	33,7±3,9	32±2,8	32±3,1	29,2±1,3	0,001
CA (cm)	89±5,5	87±4,6	85±6,7	81±6,2	0,000
Porcentaje graso (%)	19±4,4	17±3,8	17±3,8	14±1,4	0,001
Porcentaje muscular (%)	25±5,1	28±9,4	23±2,3	35±3,8	0,000
Fuerza (kg)	30,3±2,7	35,9±5,2	28±3,6	38,2±8,4	0,001
Sarcopenia (%)	31 %	24 %	38 %	19 %	0,001
Circunferencia pantorrilla (cm)	32 ± 9,3	36 ±6,4	31,3±5,6	48,2±4,2	0,003
Vo2 estimado (ml/kg/min/o2)	13,2 ± 5,2	15.7±3,3	11,5±4,7	16,9±3,3	0,002
Fatiga (FACT-F)	17,3 ± 3,8	10,4±2,5	19,6±4,2	9,4±3,1	0,012
Calidad de vida	61,7 ± 10,4	69,5±14,4	76,5±7,4	106±7,6	0,005
Distancia recorrida (m)	363±25	407±39	332±20	417±29	0,000
FCM en prueba esfuerzo (lpm)	150±4,6	152±8	152±3,5	155±7	0,012
Disnea pos (TC6M)	8±3	5±1	9±2	4±1	0,000
Fatiga pos (TC6M)	8±1	5±2	8±1	3±1	0,003

4. Discussion

Defining the correlation between existing techniques to improve quality of life, fatigue, and sarcopenia in breast, prostate, and colorectal cancers is a challenge for health professionals, because it involves an exhaustive review and interpretation of the significant findings in the theoretical and practical part of daily life. Likewise, the analysis and comparison after the implementation of two types of training such as continuous training MICT and HIIT provided information that allows a direction of training in these cases. In this order of ideas, a study of similar methodology and results carried out by Mijwel S *et al.* [25] compared the effects of resistance and interval training at high intensity and interval training at moderate aerobic and high intensity, with the study population being women with breast cancer who underwent chemotherapy. Measurements were taken at baseline and at 16 weeks. In relation to the present study, more measurements were performed in order to have more control over variables that could impact on the quality of life of patients. More tests were performed to achieve greater precision. Based on the tests' results, participants who experienced fatigue showed an improvement in their physical condition after physical training. Likewise, those who presented good conditions initially showed improvements in terms of fatigue, quality of life, and sarcopenia.

In comparison and similarity to a study conducted in Canada with breast cancer patients, using three groups: supervised aerobic interval training (AIT), supervised continuous moderate exercise training (CMT), and an unsupervised control group (NOC). For 6 weeks, AIT exercised between 70% and 100% of VO_2 peak, while CMT exercised between 60% and 70% of VO_2 peak. The results of this study showed that these programs could increase peak VO_2 and that the addition of a strength training decreased sarcopenia and improved the overall condition of the participants [26].

On the other hand, this type of physical training had already been studied previously by a team of doctors and physiotherapists in Spain in 2016, where the effects of MICT and HIIT were compared, but it was applied in patients with coronary artery disease. They HIIT should be applied because it leads to a greater increase in functional capacity compared to MICT. Hence, this logic can also be applied to our study since like cardiovascular disease, cancers is one of the main contributors of morbidity and mortality rates in different countries [27]. With that said, it is also noteworthy that most studies show that HIIT is more physically demanding than MICT, with people reporting greater enjoyment due to its time efficiency and constantly changing stimulus, as evidenced in a study by Thum *et al.* in 2017 [28]. Therefore, it is clear that structured and sequenced training can be a viable approach to improving quality of life, fatigue, and sarcopenia.

However, these types of training are generally based on the cardiovascular component with little elements of strength training, which was demonstrated by Schulzy *et al.* [29]. Therefore, in the present study, different variables were studied in depth and followed up to analyze the long-term effects, and these could serve as parameters for future research, such as the type of training, intensity, modality, rest time, training cycles, and many other attributes related to physical training, which could be interesting lines of research to cover in order to find out the respective benefits and impact on the cancer patient.

5. Limitations of the study

It is important to highlight that it is common for certain limitations to arise in this type of research due to the multiple variables that exist around the patient's oncology. For example, pharmacological treatment and diet were not included as variables to be evaluated even though they are inevitably a predominant factor in the cardiovascular, respiratory, and metabolic response to physical exercise in this type of population.

In the study population, MICT and HIIT training undoubtedly improved all the variables evaluated, especially quality of life, fatigue, and sarcopenia. The improvements were more notable in the HIIT group,

Disclosure statement

The authors declare no conflict of interest.

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