PHYSICAL ACTIVITY, EXERCISE AND CANCER

ORIGINAL ARTICLE

Protocol of the oncological physical exercise unit of the province of Alicante

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ABSTRACT

The Oncological Physical Exercise Unit (UEFO) of the province of Alicante, was created by the Spanish Association Against Cancer and Kinetic Performance (EBT of the University of Alicante) with the aim of promoting healthcare, educational and research activities focused on the benefits of physical exercise in oncological disease and its impact on the quality of life of patients, and together with the better tolerance of oncological treatments. The Unit is made up of members of the GICAFD research group of the University of Alicante and professionals with professional experience in different areas of health and physical exercise.
Keywords: Physical activity, Exercise oncology, Healthcare, Quality of life, Oncological treatments, Educational activities.

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INTRODUCTION

The Oncological Physical Exercise Unit (UEFO) of the province of Alicante, was created by the Spanish Association Against Cancer and Kinetic Performance (EBT of the University of Alicante) with the aim of promoting healthcare, educational and research activities focused on on the benefits of physical exercise in oncological disease and its impact on the quality of life of patients, and together with the better tolerance of oncological treatments. The Unit is made up of members of the GICAFD research group of the University of Alicante and professionals with professional experience in different areas of health and physical exercise.

There is scientific evidence that shows that physical exercise is essential for patients to recover the functionality and energy they had before the treatments (in the references). Furthermore, for two decades there has been a call for clinical trials evaluating physical exercise in patients with cancer, which can be beneficial and safe in most types of cancer (see Spence et al., 2010 and Tiernan, 2004 for reviews). However, many patients do not know very well what they should do or where they can go. For this reason, in the Spanish Association against Cancer (AECC) of the province of Alicante, and Kinetic Performance (EBT of the University of Alicante) we have created the first Oncological Physical Exercise Unit in the province of Alicante, in order to provide support to patients.

EVALUATION CRITERIA PRIMARY ENDPOINTS

To evaluate the effect on the functional capacity and quality of life of cancer patients through a supervised physical exercise program for 12 weeks.

Secondary endpoints:

- Increase in VO_{2max} as a beneficial effect on cardiovascular capacity.
- Changes in maximum and elastic-reactive force as indicators of muscular performance.
- Changes in body composition: lean mass and fat mass.
- State of well-being/quality of life.
- Effect of the application of the training program through the correlation of the variables of anamnesis data and clinical history.

STUDY-PROGRAM DESIGN, PARTICIPANTS AND PROCEDURES

The study-program will be an uncontrolled trial that will use a pre-post design, with evaluations at the beginning and after the intervention (12 weeks). The study will be carried out between January 2024 and March 2024 at the Oncological Physical Exercise Unit of the Spanish Cancer Association in Alicante, Spain. This process will be repeated in the remaining quarters of 2024.

This Oncological Physical Exercise Unit has a healthcare service, and is integrated as one more care in the fight against cancer financed by the Spanish Association against Cancer of Alicante, providing free clinical physical exercise services for approximately 60 people with cancer each year.

Sample size

We will need to enroll 60 patients (15 patients each quarter of the year 2024) to detect a clinically important change in VO_{2max} from baseline to post-intervention of 3.39 (±6.7) ml/kg/minutes at 80% power , assuming 15% dropout and a combrach alpha of .05. The estimated change is 3.39 (±6.7) based on a meta-analysis

of the effects of exercise on CRF in breast cancer patients and survivors. Along with an improvement in body composition and strength.

Eligible patients with cancer from any hospital in the province of Alicante will be informed about the study by their oncologist during control visits.

Potentially, eligible participants will be referred to the Spanish Cancer Association in Alicante, Spain, where a health worker will be responsible for triaging patients into different support services, including physical exercise. Patients will be eligible for the study-program by presenting these criteria:

1. The subject is able and willing to follow the procedures of the described protocol.
2. Participants must be 18 years old or older.
3. Participants will have been diagnosed with any locally or regionally advanced primary cancer.
4. Have received adjuvant chemotherapy or adjuvant radiation therapy after chemotherapy.
5. Subjects are able to walk 500m without rest.
6. They do not present any serious physical impairment, nor effects related to cancer treatments such as weakness, fatigue, changes in body composition and/or pain.
7. They do not have any physical or psychological disability,
8. The American Thoracic Society Criteria for performing a cardiopulmonary exercise test (CPET) will be met. The final determination of eligibility will occur at the time of the initial aptitude test.

EXERCISE PROGRAM

The exercise program will be designed and carried out by a Graduate in Sports Sciences with a specific qualification, in accordance with what is indicated in the Exercise guidelines for cancer survivors: consensus statement from an international multidisciplinary roundtable (Cambell et al., 2019) The exercise program will be individualized based on initial fitness testing, including cardiopulmonary fitness, muscle strength, and body composition. Participants will be asked to complete a supervised, progressive, twice-weekly, 12-week program with multi-component exercises. Each exercise session will consist of a warm-up at 50% of maximum oxygen consumption (VO_{2max}) for 5 minutes, followed by 40 to 50 minutes of the main exercise phase and then a 5-minute cool down and stretching for 5 minutes.

Cardiovascular exercise can be done on an elliptical, stationary bike, treadmill, or rowing machine. Intensity will be monitored by a PolarH10 heart rate monitoring device (Polar Electro, 2021) and will gradually be increased during the 12-week program as established in the exercise protocols.

Strength exercises will be performed with multipurpose load-bearing material, and may also be performed with machines that include chest press, leg press and multifunctional machines. The intensity of the resistance will be gradually increased during the 12-week program and will include a new maximum strength test in the sixth week of the program. Apart from the supervised sessions twice a week, from the fifth week, 1 individualized session will be held to encourage training at home.

Nutritional guidelines will be recommended for each patient based on an assessment of body composition at the beginning of the program.

Although the exercise program will be individualized, the study-program will mainly develop exercises based on group objectives. For patients with low or normal muscle mass, the program will focus on building muscle mass. For patients with normal muscle mass and high fat mass, the program will focus on fat loss. The

program design will be the same for both groups. In terms of structure; However, different starting points will be used in exercise intensity for aerobic endurance.

Different starting points of exercise intensity will be prescribed in its aerobic resistance component, to align them with the patient's personalized goal. For those patients focused on gaining muscle mass, the resistance intensity progression will be every 3 weeks. It will begin with 2 sets of 12 repetitions at 70% RM and progressing to 3 sets of 10 repetitions at 75% RM (week 3), 4 sets of 8 repetitions at 80% RM (week 6) and 4 sets of 8 repetitions at 85% RM (week 9). Regarding the cardiovascular exercise program, the intensity will progress every 4 weeks. It will start from 45% to 65% MHR (weeks 1-4), from 65% to 85% MHR (weeks 5-8) and from 85 to 100% MHR (weeks 9-12). For those patients focused on fat loss, resistance intensity progression will be every 3 weeks starting with 2 sets of 12 repetitions at 65% RM and progressing to 3 sets of 10 repetitions at 70% RM (week 3), 4 sets of 8 repetitions at 75% RM (week 6) and 4 sets of 8 repetitions at 80% RM (week 9). Regarding the cardiovascular exercise program, the intensity will progress every 4 weeks from 60% to 70% MHR (weeks 1-4), from 70% to 85% MHR (weeks 5-8), and from 85% to 100% MHR (weeks 9-12).

VALUATION UNIT

Health-related physical fitness assessments will be completed at baseline and post-intervention, and all patients will be informed of the results. Baseline testing will be performed during adjuvant therapy, while post-intervention testing will be completed during or after adjuvant therapy.

ANAMNESIS

The first test will collect the patient's characteristics, demographic and behavioral variables, which will be evaluated through self-report. Medical variables will be extracted from medical data. Patient characteristics will be evaluated to predict the influence of exercise. This exercise will be related to the response to the treatment modality (chemotherapy versus radiotherapy), and the type of cancer (breast versus other). In addition to the comparison in the objective of the exercise program (fat loss versus muscle gain), in reference to BMI (≤25 vs. 25+), and age (<50 vs. 50+).

ASSESSMENT OF BODY COMPOSITION

The second test will determine body composition. It is a measure of energy, nutritional, functional and health balance that is widely used in clinical research and field studies (Hooshmand et al., 2021; Jung et al., 2020; Fernández-Lao et al., 2013) The evaluation instrument will be the Inbody 770 (Microcaya, 2016 S.L), a device with multi frequency direct segmental bioelectrical impedance, which takes 60 seconds to obtain measurements of weight, body mass index, lean body mass, skeletal muscle mass, fat mass, body fat, muscle and skeletal index, and waist-hip ratio. To standardize body composition measurements, patients will be asked to follow some nutritional recommendations. Furthermore, body composition measurements have been observed to correlate with parameters of cardiorespiratory function such as VO_{2max} in cancer (Hooshmand et al., 2021; Bortolozo et al., 2021).

ASSESSMENT OF THE WELFARE STATE

It has been widely determined in the scientific literature that physical exercise, prescribed appropriately (Cambell et al., 2019), can increase the feeling of well-being and improve the feeling of fatigue in different

types of cancer (Desbiens et al., 2017; Gopalakrishna et al., 2017; Lewis et al., 2007). In the third test, quality of life will be measured using the Functional Assessment of Fatigue by Cancer Therapy scale (FACT-F)26, which includes the FACT-General scale (Cella et al., 1998; Cella et al., 1993). (FACT-G) is a Fatigue subscale. FACT-F consists of 40 items including 27 items for the FACT-G scale and 13 items for the fatigue subscale (FACT-F). The FACT-G includes the 4 subscales of physical well-being, functional well-being, emotional well-being, and social well-being. Higher scores on the FACT-F, FACT-G, and fatigue subscale indicate better Quality of Life/less fatigue. The minimum important difference for the FACT-F, FACT-G and fatigue subscales are 7, 4 and 3 points, respectively.

ASSESSMENT OF QUALITY OF LIFE

In the fourth test, the health status will be measured using the Life-5 Questionnaire test (EQ-5 (Ramos-Goñi et al., 2018, Herdman et al., 2011). EQ-5 is an instrument that assesses generic quality of life developed in Europe and widely used in cancer patients. The EQ-5 consists of 1 question for each of the 5 dimensions including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Higher scores on the EQ-5 indicate better health and quality of life outcomes. The minimum important difference in EQ-5 is 4 points. The EQ-5 questionnaire has recently been used in the evaluation of quality of life through physical exercise in cancer patients in Spain (Gil Herrero et al., 2022a; Gil Herrero et al., 2022b).

ASSESSMENT OF MUSCLE PERFORMANCE

The fifth test is about Maximum Strength, which is the ability to exert maximum force against external resistance and requires a maximum voluntary contraction. Patients will be evaluated using the TKK dynamometer, performing an isometric grip of 6 seconds duration, in three repetitions and with a rest of 30 seconds between measurements. Likewise, leg strength will be collected through a CMJ jump, in three attempts and with 30 seconds of recovery. Additionally, maximum strength can be collected through chest and leg press exercises using a maximum of 3 to 5 repetitions (RM), following the ACSM protocol and the Mayhew formula to predict 1RM. Muscle performance is compromised in cachexia and pre-cachectic states in cancer (Dalise et al., 2020). Due to a possible anti-inflammatory effect, physical exercise can be used as a preventive treatment (Gould et al., 2013; de Lima et al., 2008; Petersen and Pedersen, 2005). Studies have also been carried out in elderly patients to prevent loss of muscle performance, with positive preliminary results (Rosero et al., 2020; Arrieta et al., 2019).

ASSESSMENT OF CARDIORESPIRATORY CAPACITY

The sixth test will measure the ability of the circulatory and respiratory systems to supply oxygen to the mitochondria of skeletal muscle in energy production during physical activity. To do this, a submaximal treadmill test will be used to estimate maximum oxygen consumption (VO_{2max}), the volume of oxygen will be recorded using a gas analyzer meter (Metalyzer Sport, CORTEX Biophysik GmbH, Leipzig, Germany) and will be used to predict maximum oxygen consumption in milliliters per kilogram per minute, relating to VO_2 and heart rate. The parameters will have a sampling rate of 15 seconds. The protocol will be carried out in accordance with ATS CPET criteria. In patients with lung cancer, a spirometry test will be completed to evaluate lung function.

Patients will begin with a 2-minute warm-up (3.5 km/hour) and a gradual increase in speed of 0.1 km/hour every 15 seconds and an increase in incline of 0.5% every 30 seconds. The Bruce protocol will be used for patients who will not be able to walk at 4 km/hour. Perceived effort will be measured using the Borg scale

every minute in both protocols. The determination of submaximal VO_2 is a parameter widely used in interventions to evaluate the improvement of cardiorespiratory capacity in various types of cancer (Maginador et al., 2020; Spence et al., 2013).

AUTHOR CONTRIBUTIONS

All authors have contributed equally to all sections of this article.

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No funding agencies were reported by the authors.

DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

NOTE FROM THE AUTHORS

This protocol is a replica of one of the protocols used in the Exercise Oncology Unit of the Spanish Cancer Association, in Madrid, Spain. The Exercise Oncology Unit is a cancer-specific community-based facility funded by the Spanish Cancer Association in 2018.

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