



Universidade Europeia

Feasibility and functional fitness impact of a face-to-face versus home-based supervised physical exercise program in women with breast cancer after treatment: a pilot study

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Abbreviation

CB- Center Based

BC- Breast cancer

HB- Home Based

RCT- Randomized Controlled Trial

CHVNG/E- Vila Nova de Gaia / Espinho Hospitalar Centre

AICSO- Oncology Support Care Research Association

GLOBOCAN- Global Cancer Observatory

ACSM- American College of Sports Medicine

ESSA- Exercise Sports and Science Australia

PAGA's- Physical Activity guidelines for American's

Min/week- minutes per week

Mm/hg- millimeters of mercury

Hb- Hemoglobin

CTCAE- Common terminology criteria for adverse effects

CPET- Cardiopulmonary exercise test

RPE- Borg Rating of Perceived Exertion

HRR- Rest Heart Rate

BMI- Body mass index

WHO- World Health Organization

ROM- Range of motion

M0- Baseline

M1- Post Intervention

Resumo

Introdução: A relevância da atividade física com terapia coadjuvante do cancro tem vindo a ser comprovada em vários estudos. Além da distância e dos custos, a pandemia do COVID-19 criou mais uma barreira ao exercício, tornando mais difícil o acesso a programas de exercício físico supervisionados em contexto presencial. As intervenções em contexto à distância, via internet, garantem a supervisão de programas individualizados e cientificamente validados, podendo ser uma maneira segura e eficaz de proporcionar o acesso a estes programas, a pacientes com cancro de mama, mantendo-os motivados. Este é um desafio das equipas multidisciplinares que acompanham estas pessoas.

Objetivo: Este estudo teve como objetivo analisar a viabilidade, aceitação e eficácia de uma intervenção de exercício supervisionado de 8 semanas, em modo presencial (que é considerado o estado da arte) e modo supervisionado remotamente, em pacientes sobreviventes de cancro da mama, após tratamento primário, com intenção curativa. Os *outcomes* secundários incluíram medidas antropométricas (perímetro da anca, cintura, crural médio e bicipital) e aptidão funcional (força dos membros inferiores, força dos membros superiores, equilíbrio estático e flexibilidade)

Método / Desenho: Este foi um estudo piloto randomizado controlado de 8 semanas com um total de 12 pacientes do sexo feminino, 33-65 anos, com diagnóstico de cancro de mama entre os estágios Ia-IIIa. Antes das avaliações iniciais, as participantes foram randomizadas para grupo presencial supervisionado e grupo *homebased* supervisionado remotamente com uma prescrição de exercício igual: 2 dias por semana de treino combinado (aeróbio, resistência e flexibilidade) e 1 dia de treino aeróbio, com pelo menos um dia de descanso entre cada sessão.

Resultados: Não existiram abandonos durante a intervenção, logo a taxa de retenção foi de 100% nos programas supervisionados presencial e *homebased*. A adesão à duração do treino aeróbio teve um valor médio de 83%, em todos os participantes. Entre os grupos variou em entre 80% a 86%, *homebased* e presencial, respetivamente. A taxa de adesão ao volume prescrito (séries x repetições) de treino de força, teve um valor de $74\% \pm 28,2\%$, em toda a amostra. O grupo *homebased* apresentou valor um médio de $72,7\% \pm 39,2\%$ e o grupo presencial um valor médio de $75,4\% \pm 14,6\%$. A taxa de adesão à frequência foi de 82,6% no grupo *homebased* e 80,6% no grupo presencial. Após a intervenção de 8 semanas, os grupos *homebased* e presencial melhoraram significativamente a força de prensão manual do lado não operado (grupo *homebased* $3,33 \pm 2,06$ $p < 0,05$; grupo presencial $3,33 \pm 1,50$). Melhoria

significativa também foi observada favorecendo o grupo presencial no teste “*sit to stand 30''*” com aumento do número de repetições ($3 \pm 2, p < 0,05$) e diminuição do perímetro da anca ($-3,08 \pm 2,44, p < 0,05$).

Conclusão: Os resultados indicam que o protocolo On4Rehab foi viável e seguro para seus participantes. Também mostrou potencial para melhorar a aptidão funcional (força de membros superiores e inferiores) e medidas antropométricas (perímetro da anca). Os resultados são encorajadores para continuar a aplicar este tipo de programa de exercício combinado supervisionado de 8 semanas em amostras maiores, em estudos controlados randomizados e avaliar a sua viabilidade e efeito nos resultados de aptidão funcional.

Abstract

Background: The relevance of physical activity as a co-adjunct cancer therapy has been proven in numerous studies. In addition to distance and costs, the COVID-19 pandemic created yet another barrier to exercise, making access to supervised center-based (CB) exercise programs more difficult. Web-based interventions, ensure supervision of scientifically validated tailored programs, and can be a safe and effective way to deliver exercise to breast cancer (BC) patients, keeping them motivated. This is the challenge for the multidisciplinary teams who accompany these people.

Purpose: This study aimed to analyze the feasibility, acceptability, and effectiveness of an 8-week supervised exercise intervention, in face-to-face mode (which is considered state of art) and remotely supervised mode, in BC survivor's patients, after primary treatment with curative intent. Secondary outcomes included anthropometric measures (hip, waist, middle crural and bicipital circumferences) and functional fitness (lower limb strength, upper limb strength, static balance, and flexibility)

Methods/Design: This was an 8-week pilot randomized controlled study with a total of 12 female patients, 33-65 years, diagnosed with breast cancer between stages Ia-IIIa. Before baseline assessments, participants were randomized to supervised CB and remotely supervised home-based (HB) groups with a similar exercise prescription: 2 days per week of combined training (aerobic, resistance, and flexibility) and 1 day of aerobic training, with at least one day of rest between each session.

Results: With no dropouts during the intervention, the retention rate was 100% in CB and HB supervised programs. The adherence to duration of aerobic training had an average value of 83%, in all participants. Between groups it varied in a range from 80% to 86%, HB and CB, respectively. The adherence rate to the prescribed volume (sets x repetitions) of strength training, had a value of $74\% \pm 28.2\%$, in all sample. The HB group had an average value of $72.7\% \pm 39.2\%$ and the CB group an average value of $75.4\% \pm 14.6\%$. The adherence rate to frequency, was 82.6% in HB group and 80.6% in CB group. After the 8-week intervention, the HB and CB groups had significantly improved handgrip strength on the non-operated side (HB group 3.33 ± 2.06 $p < 0.05$; CB group 3.33 ± 1.50). Significant improvement was also observed favoring the CB group on the sit to stand 30'' test with increase of the number of repetitions (3 ± 2 , $p < 0.05$) and decrease on the hip circumference (-3.08 ± 2.44 , $p < 0.05$).

Conclusion: Results indicate that the On4Rehab protocol was feasible and safe for its participants. It has also showed potential to improve functional fitness (upper and lower limb

strength) and anthropometric measures (hip circumference). The results are encouraging to continue to apply this type of 8 week supervised, combined exercise program in larger samples, in randomized controlled trials (RCT), and assess their feasibility and effect on functional fitness outcomes.

Keywords: breast cancer, exercise, home-based, telehealth, feasibility, outcomes

Introduction

This research project results from a synergy between Universidade Europeia, the Vila Nova de Gaia/Espinho Hospital Center (CHVNG/E), and the Oncology Support Care Research Association (AICSO).

AICSO aims to develop and support training and research in supportive care in oncology. In this context, the ONCOMOVE program appears in 2018. It includes several research projects, training, and community action projects, including physical exercise in the path of cancer patients (before, during, and after the disease). These projects are multidisciplinary, based on the most actual scientific evidence, and mainly, patient centered. Regarding breast cancer, the MAMAMOVE program was created and has been developing and supporting research and training projects for the medical community, to support the implementation of social initiatives for education and physical exercise among patients undergoing ambulatory follow-up and inserted in the community.

Given the epidemiological situation caused by COVID-19, several difficulties have arisen in the normal functioning of the ongoing projects. The need to find alternative and more facilitating ways for people to access them arose, thus eliminating barriers to practice physical exercise and enabling these interventions to reach a higher number of people.

For this purpose, was analyzed the possibility of performing remote exercise with synchronous monitoring by exercise physiologists and, a research protocol with the designation On4Rehab was created. The name was based on the meaning of “On” as an abbreviation for online and at the same time with the meaning of “ready”, “prepared”, “fit”; of “4” which is phonetically identical to “for”, with the meaning “for” the rehabilitation process (Rehab) that arises after the disease treatment phase.

As the main objective, this study protocol aimed to verify whether a remotely supervised physical exercise intervention is feasible and, as a secondary objective, whether the effects on anthropometric, physical, and functional fitness variables derived from its implementation are similar to those of a supervised intervention in a face-to-face context (which is considered state-of-the-art) in post-treatment breast cancer patients.

Study variables (feasibility, anthropometric, physical, and functional fitness) were selected from a broader set of variables. Cardiorespiratory fitness, quality of life, quality and quantity of physical activity) will be analyzed in other studies to be carried out.

By participating in a program with these characteristics, the participants are involved in supervised physical activity programs appropriate to their anamnesis, health status, physical fitness, among others, to promote the improvement of physical and functional fitness, quality of life, as well as to reduce the sensations of the adverse effects caused by the treatments, thus helping in their rehabilitation process.

This is a very actual theme, more specifically in women, in which breast cancer is the most diagnosed type of cancer (Siegel et al., 2020). It is estimated that, in Portugal, according to the Global Cancer Observatory (GLOBOCAN, 2018), there are about 7000 new cases of breast cancer per year, in all ages. Breast cancer is the most prevalent cancer among women, of all ages. These numbers are expected to fluctuate a little by 2040. In any case, according to Mctiernan et al. (2018) and Campbell et al. (2019), the number of cancer survivors in the world is increasing. This is also proven by Siegel et al. (2020). This is due to good practices both in terms of prevention and in terms of the evolution of treatments. Since the '90s, the importance of exercise in physical indicators related to cancer has been considered and since then its increasing relevance has been shown before, during, and after cancer treatment. Exercise is now highly recognized as a non-pharmacological co-adjuvant treatment (Courneya et al., 2014; Idorn & thor Straten, 2017; Iyengar & Jones, 2019), in addition to being recognized in the literature as an important way of prevention of various types of cancer (Mctiernan et al., 2019).

The 2010 American College of Sports Medicine (ACSM) roundtable was one of the first reports to conclude that cancer survivors could safely conduct exercise programs to improve physical fitness and restore physical function, improve quality of life, and mitigate cancer-related fatigue. A second ACSM roundtable was convened in 2019 for advanced exercise

recommendations as well as specific recommendations by type of cancer and expected results (Campbell et al., 2019a). ACSM has launched exercise guidelines for cancer survivors recommending 150'/week of moderate-intensity aerobic activity (divided into at least 3 days a week, for 6-12 weeks), and, two or more days per week of strength training with moderate to vigorous intensity, and daily stretching of major muscle groups when possible. A prior assessment and prescriptions adapted to each person/situation are recommended, meaning, tailored to each case, based on numerous factors: type of cancer, stage and prognosis, treatment history, current and future treatments, symptoms and side effects of the disease and treatment, current health status and physical fitness, as well as the individual goals of the person. Hayes et al. (2019), in Exercise and Sports Science Australia's (ESSA) position statement, concluded that for most of cancer patients, multimodal, moderate to high intensity exercise will be appropriate, but there is no set prescription and total weekly dosage that would be considered evidence-based for all cancer patients. There is a need to tailor the programs to each person's needs, to reduce the risk of being harmful. According to Nilsen et al. (2018), "the most important methodological consideration when designing an exercise RCT is consideration of fundamental components of an exercise prescription (e.g., frequency, intensity, and modality) and principles of training", to show precise exercise dose" and most of the times, there is lack of information about it. This has high relevance because it may provides better context for interpreting the studies and improve the quality of future interventions (Bland et al., 2021). Newton et al. (2020) refers that exercise in people with cancer serves to improve the quality and quantity of life by reducing, preventing, or reversing treatment sensations related to toxicities; mitigation of cancer-related fatigue and its treatments; and recovery of physical function lost during the treatment phase. Cannioto et al. (2021) analyzed the correlation between breast cancer recurrence and mortality, and the compliance pre and post diagnosis, with the Physical Activity Guidelines for Americans (PAGA's), that recommend at least 150' of moderate aerobic exercise and two days of strength training per week. This analysis was performed at 4 different times: during treatment and after treatment at 6 months, 1 year and two years. They found that compliance with these guidelines is directly related to a decrease in the rate of recurrence and mortality. In addition, patients reporting lower volumes and intensity of activity experienced similar overall survival advantages as those who met the PAGA's. Programs between 6 and 12 weeks have shown benefits in symptoms with strong evidence in outcomes such as fatigue, anxiety, depression, physical function, lymphedema, and health related quality of life, associated with cancer treatments (Campbell et al., 2019b).

Taking into account all these benefits, the access to these programs must be as easy as possible. The Internet is a powerful medium for providing accessible and low-cost resources to address unmet support needs in cancer survivorship (Rogers et al., 2017).

Phillips et al. (2019) analyzed the preferences of patients in physical activity programs provided via remote. The themes that had the highest interest rate were relevant to content related to the theme "exercise news" and "news from studies related to breast cancer"; agenda to book/change sessions as well as the possibility to record sessions. The results, highlight the need to develop easy-to-use, motivating, and specific services for breast cancer survivors. In another study, Lloyd et al. (2020) highlighted the variety of preferences among participants. They recognize the importance of these types of programs but have observed many different preferences among participants. With this type of approach, HB exercise may be able to overcome some barriers that tend to be seen as limiting adherence/retention to this type of program because it can be individualized, it can have live supervision, it can meet current guidelines for social distancing avoiding risky contacts for these people, great conditions are not necessary for its realization and its cost are also lower (Bland et al., 2020). The lack of corrective feedback, the lack of training structure, the lack of prior education and the lack of supervision were identified as the main difficulties experienced in this type of intervention. (Bland et al., 2020). Newton et al. (2020) refer to some practical recommendations for patients in order to improve the functioning of the programs, such as the appointment must be made to schedule the session at the possible / desired time; they should prepare a suitable and safe environment for exercising at home; prepare the necessary material for the session (mattress, towel, water, music) and the material for viewing the session (smartphone, tablet, computer, television). According to the authors, meeting the interests and needs of the participants can bring advantages regarding the retention of programs.

RCT's, with remote supervised exercise programs, tailored to each participant and based on the ACSM guidelines for cancer survivors, showed that these online interventions can have encouraging results on functional fitness, and be an effective alternative to face-to-face interventions. Galiano-Castillo et al. (2016) in addition to improvements in the strength of the upper and lower limbs, they also obtained high retention rates in a study with these characteristics. Ariza-Garcia et al. (2019) adopted the same type of approach and verified positive results in adherence and improvement of physical capacity, comparable with the results obtained in interventions with face-to-face supervision. In this intervention, the

individualization of training plans, tailored to the participants, and the use of social media tools such as (conversational chats, messages, e-learning, video calls, activity trackers) was a concern.

In a recent systematic review that included results from 80 RCT's, Neil-Sztramko et al. (2019) concluded that most of the studies in this area do not attend to all principles of exercise training recommendations (specificity, progression, overload and initial values) neither report all components of the exercise prescription (duration and exercise intensity) in the methods. The adherence to the prescription in the results that helps to understand if the prescribed exercise dose is feasible, is also an identified gap. All this precludes transparency and replicability of clinical trials in this population.

Objectives

Taking into account the topics covered, three hypotheses arise:

Hypothesis 1: The HB exercise program with synchronous supervision is feasible as the supervised CB exercise program in women with breast cancer in post treatment phase?

Hypothesis 2: The HB exercise program with synchronous supervision promotes similar improvements on functional fitness as the supervised CB exercise program in women with breast cancer in post treatment phase?

Hypothesis 3: The HB exercise program with synchronous supervision promotes similar improvements on body circumferences as the supervised CB exercise program in women with breast cancer in post treatment phase?

Thus, the primary aim of this study is to assess the feasibility and acceptability of an 8-week HB exercise program with remote supervision and CB, both with supervision. The secondary aim is to assess the impact on functional fitness (lower limb strength, isometric handgrip strength, flexibility, and static balance), and on anthropometric measures (hip, waist, middle crural and, bicipital circumferences).

Methods

Study Design

A randomized controlled study with an intervention time of 8 weeks was conducted, with pre and post-intervention physical assessment. Before the start of the intervention, the participants were also subjected to a physiatry assessment and a psychological assessment to better know the individual needs of each participant. The clinical history was also available to the exercise physiologist since the beginning of the process to better tailor the intervention (presence of comorbidities; disease history and the treatment performed by participants and current medication).

The CB intervention took place in the premises of the League of Friends in the CHVNG / E; HB group carried out the intervention in their homes, with remote supervision, via Zoom App. Both groups were under the same exercise prescription. This study was approved by the Ethical Commission of CHVNG/E with the registry number 06/2021.

WhatsApp application was a social media tool used to improve retention and adherence to the program. It was used as a chat room between the participants of the HB group and the physiologists, to share information about the relevance of the exercise. It was also used to share sensations and feelings of the participants among themselves and with the physiologist and to schedule or change sessions appointments.

The training principles and variables, as well as the progression that are present in the exercise prescription, are all described to precisely show the exercise dosage.

Participants

Participant recruitment took place in the Oncology Service of CHVNG/E. Trial participants were recruited from March 2021 until the number of 12 was achieved in June 2021. One drop out happened before the start of the intervention, due to unavailability to belong to the allocation group. This participant was substituted so the intervention could have the number of 12. All participants had to read and sign, in case of agreement, a consent form where all the steps of the intervention were explained as well as potential benefits and risks. Participants were then blindly randomized in a 1:1 ratio and assigned to each group, before the start of the baseline assessment. This process was performed by the physiologist. The flow chart is represented in fig.1

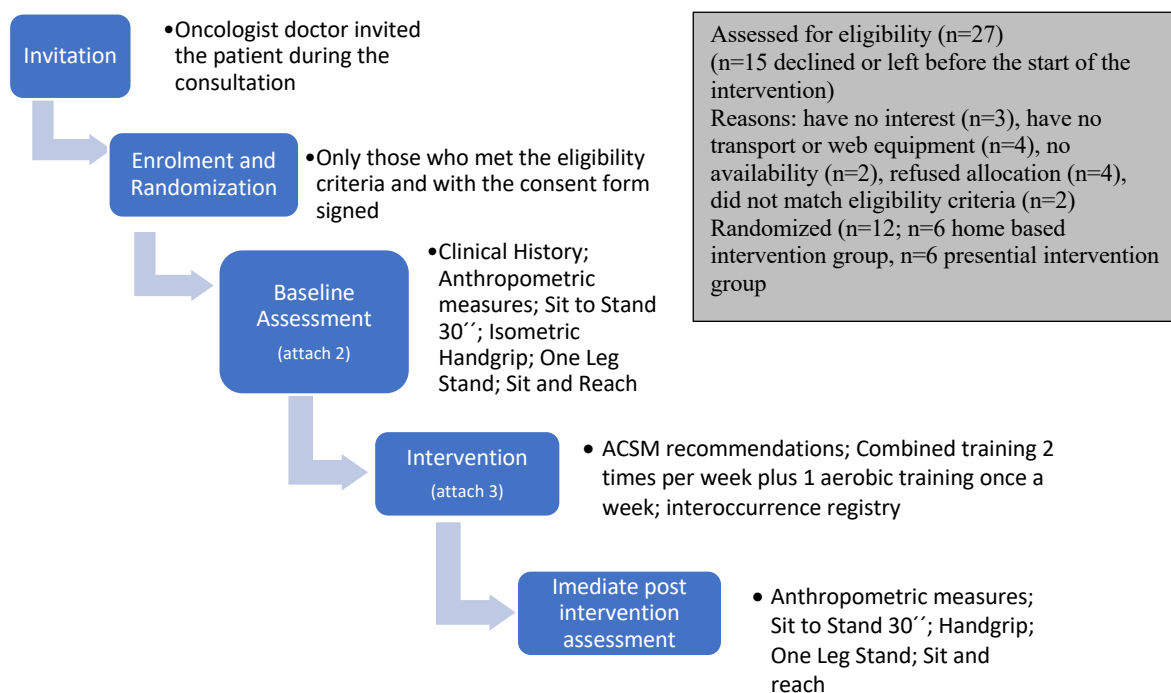


Figure 1. Program Flow

Eligibility Criteria

The inclusion criteria attended to the following: women, under the legal age, with a diagnosis of breast carcinoma between stages 0 and IIIc, ECOG performance status 0 to 1, undergoing primary treatment with curative intent (surgery associated or not, with chemotherapy and/or adjuvant radiotherapy) for at least one month, with follow-up on medical oncology consultation at CHVNG/E, with the consent of the assistant oncologist to perform physical exercise, non-compliance with current physical activity guidelines recommended by the ACSM (moderate aerobic activity ≥ 150 min/week or vigorous ≥ 75 min/week and ≥ 2 strength training/week), with cognitive ability to understand the project proposal.

The exclusion criteria were: severe anemia verified in the last 3 months ($Hb \leq 8$ g / dl) or moderate ($Hb > 8$ and ≤ 10 g / dl) symptomatic (sustained tachycardia, exertional dyspnea, chest pain or syncope), uncontrolled arterial hypertension (HTN grade 3-4 (CTCAE v.5)) (Systolic ≥ 160 mmHg and / or Diastolic ≥ 100 mmHg and / or potentially fatal consequences (malignant Hypertension, transient or permanent neurological deficit or hypertensive crisis), uncontrolled diabetes mellitus, known cardiac or respiratory pathology, any other contraindication given by the physiatrist and / or assistant surgeon.

Baseline characteristics of the participants are summarized in table 1. 12 female participants (mean age 55±9) with breast carcinoma (n=5, 41%, in stage Ia; n=2, 17%, in stage IIa; n=3, 25%, in stage IIb; n=2, 17%, in stage IIIa) met the inclusion criteria and were blindly randomized to the HB group (n=6) and to the presential group (n=6). All the participants were submitted to surgery (mastectomy n=6, 50%; breast conserving surgery n=6, 50%) with curative intention, associated with adjuvant treatment (chemotherapy n= 7, 58%, radiotherapy n =5, 42%, monoclonal antibody n= 4, 33%, and hormonotherapy n=12, 100%). All of them are still under hormonal treatment. As adverse effects of the treatments, almost all still reported articular pain (n=11, 92%), lymphedema (n=1, 8%), and peripheric neuropathy (n=3, 25%).

Table 1 - Baseline haracterization of participants (n=12)

Variable	
Age (mean)	55 ± 9
Weight HB Group	68 ± 15.6
Weight CB Group	83.4 ± 20.9
BMI HB group	26.6 ± 6
BMI CB Group	32.6 ± 6.7
Tumor Characteristics	
Stage Ia	5 (41%)
Stage IIa	2 (17%)
Stage IIb	3 (25%)
Stage IIIa	2 (17%)
Type of surgery	
Mastectomy	6 (50%)
Breast Conserving surgery	6 (50%)
Adjuvant Treatments	
Chemoterapy	7 (58%)
Radiotherapy	5 (42%)
Monoclonal Antibody	4 (33%)
Hormonotherapy	12 (100%)
Actual adverse effects	
Articular pain	11 (92%)
Lymphedema	1 (8%)
Peripheric neuropathy	3 (25%)

Intervention

The physical exercise intervention was developed under the guidelines of the ACSM for cancer survivors. To decrease the risk of bias, both groups received the same assessments and supervised exercise prescription, tailored to the specific needs of each participant at that time or indicated by the physiatrist in the baseline assessment. This was essential for enhancing adherence to the program.

Before starting the intervention, an experimental session with the HB participants was performed to ensure that there would be no problems with the use of Zoom App. The best way to place the camera was also verified, as well as the security conditions of the space where the sessions would take place. It also served to inform about the material needed for the sessions and to clarify any doubts that the participants could have.

A total of 24 sessions were included (3 sessions per week) with two combined training sessions (mobility, aerobic training, strength training, and flexibility) plus one aerobic training session, interspersed with at least one day of rest between them. In total, 16 training sessions lasting approximately 60 minutes of combined training twice a week, with moderate to vigorous intensity, and 8 sessions lasting 30 to 45 minutes of aerobic training, with moderate to vigorous intensity once a week. The intensity was individualized and defined based on the initial assessment.

The type of training proposed was prolonged and rhythmic training, which met the training typology proposed by ACSM. The structure of the training plan was based on the FITT-VP principles (frequency, intensity, time, type, volume, and progression).

Aerobic Training

Concerning aerobic training, Cardiopulmonary Exercise Testing (CPET) was performed to allow the detection of possible cardiac pathologies and to define the intensity zones. The recommended intensities were between 60-80% of the reserve heart rate or 12-15 on the subjective effort perception scale (PSE).

Resistance Training

In resistance training, the recommendation states to start with low intensity and progress slowly and consistently. The interval between 1-3 sets of 8-15 repetitions is recommended by ACSM (2019). The recommended intensity is between 12-15 PSE.

Flexibility Training

According to ACSM (2019), flexibility training should be within the possible range of joint movement. It should progress 2-3 days a week for every day giving greater focus to areas with reduced mobility.

Combined Training

Each session consisted of at least 30 minutes of aerobic training combined with strength training and flexibility. In strength training, greater focus was given to the largest muscle groups. As an accessory material, resistance elastics with handles were used. All participants had an individual record of inter-occurrences per training session to assure the safety of the intervention. In the HB group, the intensity of the aerobic training was defined and adjusted using Borg's Rate of Perceived Exertion (RPE) scale. In CB group, was used the percentage (%) of reserve heart rate (HRR). The fact that the CB group was monitored with heart rate monitors (Polar P10), allowed the use of cardio-pulmonary exercise test data to define the training intensities within the recommended intervals. The desired %HRR for each session, was calculated always with the daily value of rest heart rate. Moderate intensity, between the 40-59% HRR for the first 4 weeks, and in the last 4 weeks, vigorous intensity, between 60-89% HRR.

The workout began with general and/or specific joint mobility exercises, for about 3-5 minutes, followed by the warmup with a duration time of 10'. It consisted in aerobic exercise with a gradual increase in intensity, progressing from the subjective perception of effort (RPE) 9-11. Then gradually entering the fundamental phase of training where the intensity increased to 12-13. The fundamental part of the training consisted of 4 blocks. Each block started with 1 aerobic training exercise (5') and three strength exercises (one/two sets of 8 repetitions, in moderate intensity (12-13 RPE). In the first block, the strength exercises focused on the muscles of the shoulder, biceps, quadriceps, and buttocks; in the second block, they focused on the core, chest, and shoulder muscles, as well as balance work; in the third block the focus went to the posterior region of the trunk (dorsal, spine extensors), quadriceps and glutes; in the fourth and last block, the focus was on the triceps, chest, shoulder and abdominal. The fundamental phase had a duration of 30-40 minutes. Then, a soft cool down, decreasing the intensity to 9-11 RPE, in which the first objective was to gradually reduce the

heart rate, to prevent any sudden drops in blood pressure, by walking in place, and then performing a series of stretches, that focused on the major muscle groups.

Volume and Intensity management

The initial volume and intensity were based in the physical baseline assessments and also in the inputs from cardiology, physiatry and psychology. These inputs could be the reason to start with lower or higher volume/intensity. Every two weeks, an increase in training volume and intensity was predicted. Regarding aerobic training, the proposed progression was from moderate (12-13 RPE) to vigorous (14-15 RPE) by increasing the execution speed. Concerning strength training, the proposed progression is moderate (12-13 RPE) to vigorous (14-15 RPE) by increasing the number of proposed sets and repetitions. From week 2 to week 3, there was an increase from 2 to 3 sets of 8 repetitions; from week 4 to week 5 there was an increase in the number of repetitions with 2 sets of 15 repetitions and at the end of week 6 for week 7, an increase for 3 sets of 15 repetitions. In the HB group, the decision was based on the PSE reported by the participants, so the moment for increasing the volume and intensity was flexible. The increments were slow and gradual, adapted to the specific needs of each participant, the presence of adverse effects, and comorbidities. Flexibility training was done also in a way to promote a progressive increase in joint amplitude, always respecting the limits of anatomical integrity, performing major muscles (chest, shoulder, back muscles, quadriceps and hamstrings) 15'' stretching exercises.

Outcomes

Assessment of the primary outcomes

Primary outcomes were measured in all participants during all the intervention. The primary outcomes were feasibility and acceptability of the program and measured as follows:

- Intervention Recruitment Rate is assessed by the number of invitations made versus accepted (invitation made by the assistant oncologist).
- Program Retention Rate assessed through the number of initial vs. final participants.
- Adherence Rate assessed by the number of sessions predicted vs. missed sessions.
- Adherence Rate to the training prescription (volume), adjustments, and their reasons.

- Tolerance to training through recording of symptoms and adverse effects.
- Assessment of the reasons for absences from sessions and for dropping out of the program.

Secondary outcomes were measured in all participants in 2 different moments:

- M0 (baseline assessments): before the beginning of the intervention (maximum 3 weeks before)
- M1 (post-intervention): the week immediately after the end of the intervention

Assessment of the Secondary Outcomes

Participants were asked not to consume food or caffeine within two hours before the assessment nor participate in exercise the day before the assessments. Participants were assessed in the following parameters: characterization of the clinical history; anthropometric assessment (weight, height, body mass index (BMI), waist, hip, middle crural, and bicipital circumferences; lower limb strength, bilateral isometric handgrip strength, flexibility, and static balance.

Anthropometric assessment

HEIGHT

The height of the participants was measured with a stadiometer. Participants were asked to remove their shoes off and have nothing dressed on the head. They were then asked to remain static, with the upper members relaxed on the side of their body with feet and knees together. The evaluation was carried out by placing the stadiometer comb against the head, making a slight compression of the highest point of the skull (vertex). The value had an approximation of 0.1 centimeters (Marfell-Jones et al., 2007).

WEIGHT

Bodyweight was measured using a weight balance Tanita (model BC-545N). Participants were asked to have the minimum clothes as possible, with no accessories and without shoes. Then participants were asked to step on and remain static. The value had an approximation of 0,1Kg (Marfell-Jones et al., 2007).

All the circumferences' assessments were made under the World Health Organization (WHO, 2011) recommendations.

WAIST CIRCUMFERENCE

The perimeters were measured .in a private place, so the participants were relaxed as they were asked to remove the jersey or to put it up, to leave their abdominal area visible. The lower edge of the last palpable rib and the upper edge of the iliac crest was marked with a pen. The midpoint between these two points was defined, always on the participant's right side. The tape measure was placed at the midpoint previously recorded, parallel to the floor and the participant was asked to inhale and exhale, with the measurement to be obtained at the end of exhalation. Two measures were made and the average of both was calculated in case of a 0,5 cm difference between them. If the difference were equal or bigger to 0,5cm, a third measure was done and the average of the three was calculated.

HIP CIRCUMFERENCE

The participants were standing on their feet hip-width and barefoot. The physiologist stands on the right side of the participant. The measure was taken on the glutes area with the biggest volume. Two measures were made and the average of both was calculated in case of a 0,5 cm difference between them. If the difference were equal or bigger to 0,5cm, a third measure was done and the average of the three was calculated.

MIDDLE CRURAL CIRCUMFERENCE

The participants were standing on their feet, hip-width, and barefoot. Participants were asked not to make quadriceps contractions. The measure was made on the right leg of the area with the biggest volume.

BICIPITAL CIRCUMFERENCE

The participants were standing on their feet with the upper members relaxed. The measure was made in the area with the biggest volume of the right arm.

Functional Fitness assessment

All the following assessment procedures were made under Rickli & Jones (2013) methodology.

LOWER LIMB STRENGTH

We used the 30'' Sit to Stand Test. A chair of 43cm height was placed leaning against the wall. The test was first demonstrated by the physiologist. After it, the participant was asked to perform the test. They started seated in the chair with arms crossed near the chest and shoulders. The participant was asked to perform the maximum repetition of the movement (get up and sit down) for 30 seconds. The valid repetitions were those where the participant touched with the glutes on the chair in the sit movement and fully extended knees in the get-up movement.

HANDGRIP TEST

The handgrip test with a dynamometer was applied to measure the bilateral handgrip isometric strength; The test was firstly demonstrated by the physiologist and then performed by the participant. The dynamometer was adjusted to the size of the hand. The participants were seated in a chair and performed 3 repetitions in each hand, of 3 seconds each, alternating right and left hand, so one hand could rest about 1 minute between each try. Neither the arm/hand nor the dynamometer could touch any surface during the test execution.

STATIC BALANCE

To measure the static balance, we used the Single Leg Stance. The physiologist demonstrated the test before the participant's execution. Participants were barefoot. One try was allowed before the registration. It was asked to the participant to lift one member, for a maximum of 20 seconds. The participant should be looking to the front, with hands-on the side of the hips. Time started to count since the foot left the floor until it touched it again. Both sides were evaluated.

FLEXIBILITY

The flexibility was assessed with the Sit and Reach test. The participants were seated in a chair, one leg in 90° flexion with foot on the floor and the other extended, only with the heel

on the floor. With both hands together, participants were asked to slide down the extended leg and reach as far as they can in the foot direction and hold the position for 2 seconds. The distance between the point of the hand fingers and the point of the foot fingers was measured.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences for Windows (IBM SPSS Statistics version 27 New York, USA). Descriptive analyses were performed on all participants who were randomly assigned to each group. The Shapiro-Wilk test was applied to test the normality of the delta variables. The inter-group variation was measured with the paired-samples T-Test and the variation between the groups was measured with the independent-samples T-Test. To assess the correlation between the variable “Attendance %” and the all the other variables, Pearson correlation technique was applied. To assess the adherence to exercise prescription an analysis of the volume of aerobic training (duration * frequency) and volume of strength training (sets * repetitions) was performed. Prescribed aerobic training per session was calculated and multiplied for the number of completed sessions to provide the total volume. Prescribed strength training volume (sets and repetitions) was calculated for each individual exercise and summed to provide a total session volume. The load was not considered because working with elastic bands does not allow its quantification. Further, total volume from all sessions was summed to derive the total prescribed. Adherence to frequency, was calculated as a ratio of the number of exercise sessions performed vs the number of sessions prescribed

The changes to exercise prescription were analyzed separately into programmed (those that were already planned before training) and non-programmed (which were not planned before training). The reasons were all registered. Significance level was $p < 0,05$

Results

Characteristics of the patients in baseline were presented in table 1, in the participants chapter.

The recruitment rate was 44%, with 12 invitations accepted out of 27 made. The reasons for declining the invitation were “have no interest” (n=3, 20%), “have no transport or web equipment” (n=4, 27%), “no availability” (n=2, 17%), “refused allocation” (n=4, 27%), “did not match eligibility criteria” (n=2, 17%). The retention rate for the program was 100%. No participants dropped out the program during the intervention in both intervention groups. The

frequency adherence rate was calculated as a ratio of the number of exercise sessions performed with the number of sessions prescribed. In the HB group, we had a rate of 82.6% and in the presential group, the rate was 80.6%. The exercise adherence to the exercise prescription rate was evaluated in terms of aerobic and strength volume. The presented values refer to the 8 weeks of the intervention. The adherence to duration of aerobic training had an average value of 83%, in all participants. Between groups it varied in a range from 80% to 86%, HB and CB, respectively. Regarding strength training, the prescribed volume (sets x repetitions) was well tolerated by 74%, in general. The HB group had an average value of 72.7% and the CB group an average value of 75.4%. The adherence rate to prescription's aerobic and strength volume variables is shown in the table 2.

Table 2 - Individual analysis by variable

All Sample (n=12)			
Variables	Predicted	Performed (average)	%
Aerobic training			
Total Volume (min)	720	600 ± 140	83.3% ± 19.5
Resistance Training			
Volume (Sets x Reps)	4752	3519 ± 1341	74% ± 28.2
HB Group (n=6)			
Variables	Predicted	Performed (average)	%
Aerobic training			
Total Volume (min)	720	580 ± 198	80.6% ± 27.5
Resistance Training			
Volume (Sets x Reps)	4752	3456 ± 1861	72.7% ± 39.2
CB Group (n=6)			
Variables	Predicted	Performed	%
Aerobic training			
Total Volume (min)	720	620 ± 58	86.1% ± 8.2
Resistance Training			
Volume (Sets x Reps)	4752	3582 ± 694	75,4% ± 14.6

Dose adjustments to aerobic, strength and flexibility, and also their reasons, are summarized in table 3. Fatigue was the most evoked reason in aerobic training. 25% of the participants refer to fatigue as the cause to decrease prescribed intensity. Lower limb pain with a range

between 16.7% to 25% and upper limb pain with a range between 8.3%-50% of the participants were more prevalent in strength training. In aerobic training all the adjustments were non programmed. In strength training, the adjustments caused by fatigue were all unprogrammed. 70% of the adjustments made because of lower limb pain, 89% of the adjustments made because of upper limb pain, and 83% of the adjustments made because of lack of articular range of motion (ROM) were programmed.

Table 3 – Aerobic, Strength and Flexibility adjustments; Programmed and non-programmed adjustments

Aerobic			No of patients	%	No of sessions	%	Programmed	Non Programmed
Dose Adjustment	Physical Related							
	<i>Fatigue</i>		3	25	7	2.4		8
	<i>Lower limb pain</i>		2	16.7	6	2		2
	<i>Upper limb pain</i>		1	8.3	1	0.3		1
Strength								
Dose Adjustment	Physical Related							
	<i>Fatigue</i>		2	16.7	20	15.6		20
	<i>Lower limb pain</i>		3	25	14	10.9	14	6
	<i>Upper limb pain</i>		6	50	15	11.7	26	5
	<i>ROM</i>		6	50	14	10.9	20	4
Flexibility								
Dose Adjustment	Physical Related							
	<i>Lower limb pain</i>		2	16.7	5	1.7		4
	<i>Upper limb pain</i>		1	8.3	12	4.1	8	3

The reasons for missed sessions are presented in table 4.

Table 4 - Missed sessions and reasons

Missed sessions		Number of patients	%	Number of sessions	%
	Health Related				
	<i>Medical consult</i>	3	25	5	3.9
	<i>Dental surgery</i>	3	25	14	10.9
	<i>Flu</i>	1	8.3	4	3
	Personal reasons related	1	8.3	2	1.5

Regarding secondary outcomes, significant improvements were found both HB and CB groups for handgrip strength on the non-operated side (HB 31.33 ± 4.2 , $p < 0.05$; CB 32.17 ± 2.99 , $p < 0.05$). Significant improvement was also observed favoring the CB group for the sit to stand 30'' test (22 ± 4 , $p < 0.05$) and for the hip circumference (119 ± 15.2 , $p < 0.05$). The HB group had marginal improvements for the sit to stand 30'' test (27 ± 5 , $p = 0.061$). In addition, there were no significant differences between groups. The variations between baseline and after the 8-week intervention, in both groups, are presented in Table 5.

Table 5 - Baseline and after 8-week intervention (M1) assessments for both groups. T-Test for comparison between moments

Outcomes	HB Group	p	CB Group	p
Weight (Kg)				
Baseline	68.0 ± 15.5	.770	83.4 ± 20.9	.552
M1	67.6 ± 14.1		82.9 ± 19	
BMI (Kg/m²)				
Baseline	26.60 ± 5.99	.699	32.60 ± 6.67	.575
M1	26.38 ± 5.18		32.40 ± 5.95	
Waist circumference (cm)				
Baseline	90.4 ± 12.5	.681	100.49 ± 12	.374
M1	89.4 ± 13		99.0 ± 11.5	
Hip circumference (cm)				
Baseline	103.5 ± 9.3	.863	119.7 ± 15.2	* .027
M1	103.4 ± 7.9		116.6 ± 13.1	
Middle Crural circumference (cm)				
Baseline	52.5 ± 6.7	.926	59.8 ± 7.7	.272
M1	52.4 ± 4		61.8 ± 7.0	
Bicipital circumference (cm)				
Baseline	30.4 ± 6.1	.552	34.2 ± 5.2	.507
M1	30.0 ± 4.7		33.9 ± 4.7	
One Leg Stand right member (s)				
Baseline	14.47 ± 8.6	.207	13.91 ± 7.45	.784
M1	18.87 ± 2.7		13.26 ± 8.12	
One Leg Stand left member (s)				
Baseline	11.09 ± 9.8	.076	9.66 ± 7.36	.374
M1	19.60 ± 1		12.52 ± 8.37	
Sit to Stand 30'' (repetitions)				
Baseline	19 ± 5	.061	22 ± 4	* .030
M1	27 ± 5		25 ± 4	

Handgrip operated side (Kg)				
Baseline	30.67 ± 4.5	.130	30.50 ± 2.66	.136
M1	32.50 ± 3.7		32.50 ± 2.35	
Handgrip non operated side (Kg)				
Baseline	31.33 ± 4.2	* .011	32.17 ± 2.99	* .003
M1	34.67 ± 5.1		35.50 ± 2.95	
Sit and Reach right leg (cm)				
Baseline	-1.92 ± 6.7	.721	.50 ± 9.02	.479
M1	-1.17 ± 3.9		2.30 ± 7.50	
Sit and Reach left leg (cm)				
Baseline	3.58 ± 7.5	.170	1.80 ± 7.80	.793
M1	-.67 ± 3.5		2.10 ± 7.69	

* significant differences

Despite the variations found in both groups, no significant differences were found between CB and HB groups, as shown in table 4. ($p > 0.05$)

Table 6 – Comparison between the HB and CB groups for variables of interest (T-Test)

Variables	t	p	dif
Weight variation	.097	.925	0.16
BMI variation	-.027	.979	-0.02
Waist variation	.153	.881	0.42
Hip variation	1.956	.079	2.89
Middle crural variation	-.954	.363	-2.12
Bicipital variation	-.114	.912	-0.08
Right member OLST variation	1.338	.210	5.05
Left member OLST variation	1.177	.266	5.67
30'' Sit to Stand variation	1.349	.207	4.33
Operated member Handgrip	-.110	.915	-0.17
Non Operated member Handgrip	.000	1.000	0.00

Right member SR variation	-0.347	736	-1.05
Left member SR variation	1.174	.271	2.61

Pearson correlation technique did not demonstrate any association between the variable “attendance %” and the all the other variables ($p > 0.05$). The results are shown in table 5.

Table 7 Correlation between attendance % and all the other variables

Pearson Correlations		
		Weight variation
Attendance %	Pearson Correlations	-.135
	<i>sig. (2 tailed)</i>	.675
	<i>N</i>	12
		BMI variation
	Pearson Correlations	-.080
	<i>sig. (2 tailed)</i>	.804
	<i>N</i>	12
		Waist variation
	Pearson Correlations	.220
	<i>sig. (2 tailed)</i>	.491
	<i>N</i>	12
		Hip variation
	Pearson Correlations	-.366
	<i>sig. (2 tailed)</i>	.243
	<i>N</i>	12
		Middle crural variation
	Pearson Correlations	.147
	<i>sig. (2 tailed)</i>	.648
	<i>N</i>	12
		Bicipital variation
	Pearson Correlations	-.009
	<i>sig. (2 tailed)</i>	.978
	<i>N</i>	12
		Right member OLST variation
	Pearson Correlations	-.063
	<i>sig. (2 tailed)</i>	.845
	<i>N</i>	12
		Left member OLST variation
	Pearson Correlations	.058

<i>sig. (2 tailed)</i>	.857
<i>N</i>	12
30'' Sit to Stand variation	
Pearson Correlations	.478
<i>sig. (2 tailed)</i>	.116
<i>N</i>	12
Operated member Handgrip	
Pearson Correlations	.005
<i>sig. (2 tailed)</i>	.988
<i>N</i>	12
Non Operated member Handgrip	
Pearson Correlations	.118
<i>sig. (2 tailed)</i>	.715
<i>N</i>	12
Right member SR variation	
Pearson Correlations	.016
<i>sig. (2 tailed)</i>	.963
<i>N</i>	11
Left member SR variation	
Pearson Correlations	.339
<i>sig. (2 tailed)</i>	.307
<i>N</i>	11

Discussion

Overall retention to the program was 100%. We had no dropouts during the intervention. On4Rehab protocol retention rate is better than the results of the studies of Galiano-Castillo et al. (2016) which had a retention rate of 93% and (Macdonald et al., 2020)), which had a retention rate of 83%. This might have happened, and according to the literature, because of the concern about following ups on the sessions, hearing the participants' experiences and feelings about the program in chat conversations. The fact of being flexible in the scheduling of the sessions, allowing appointments at times that were not foreseen in the beginning also contributed to the good adherence to the program, as Phillips et al. (2019) and Newton et al. (2020) found in their studies. According to the authors, meeting the interests and needs of the participants can bring advantages regarding the retention of programs. The use of the Zoom app allowed to have the live supervision that this kind of program's need, as Newton et al. (2020) suggest. The communication and interaction between the participants, and between the participants and the exercise physiologist, before, during, and after the workouts, was also

possible with the use of WhatsApp app. This strategy made it possible to prevent the lack of corrective feedback, the lack of training structure, the lack of prior education, and the lack of supervision, which had been identified by Bland et al. (2020) as the main difficulties experienced in this type of intervention.

Enhancing the reporting of exercise prescriptions, particularly FITT adherence, may provide better understanding of the correct exercise dose, and thus provide conditions to replicate the protocols, improving future research conditions. Bland et al. (2021) in a recent systematic review that included 107 studies, concluded that only 7% fully reported adherence to the FITT prescription components.

Despite of an average of 83% of completion, the adherence rate to volume of aerobic training, has shown widespread variations and interruptions in some participants. The study of Kirkham et al. (2018), indicated by Bland et al. (2021) as a reference in the adherence report, refer to this type of events and mentions the treatments and their adverse effects as responsible for these interruptions/adjustments. If no report about this kind of events is made, the application of this studies could increase the risk of harming or participant dropout. This highlights the importance of the principle of specificity. The same about resistance training. It is fundamental to know about some variables of interest such as sets and repetitions. In this paper the variables in analysis were sets and repetitions to understand if the strength training volume was well tailored. In 74% of the cases, no adjustments in series or repetitions' number were necessary to be done. This means that the prescribed total volume of strength training was higher than the completed for 26% of the participants in some moment. Fairman et al. (2020) applied a similar method to report resistance training dose, adherence, and tolerance in patients with cancer. Kirkham et al. (2018) analyzed the adjustments made to the prescription among women with early breast cancer across the trajectory of adjuvant treatment in a 20-week supervised CB exercise prescription and in a HB exercise prescription. 15% of the sessions, needed adjustments concerning aerobic training. These were related to intensity/fatigue. In our study, the value related to this variable was 2.4% of the sessions.

In relation to secondary outcomes, we found statistically significant improvement in grip strength of the non-operated member in both groups, and significant improvements in lower limb strength and waist circumference in the end of the 8-week intervention in the CB group. Lower limb strength had marginal improves in HB group. All the other outcomes (weight, BMI, waist, hip, middle crural and bicipital circumferences, static balance, handgrip strength,

and flexibility) did not suffer significant improvements in the HB group. Same on the CB group. Macdonald et al. (2020) also found significant improvements in grip strength in a similar program (8-week intervention), based on ACSM guidelines for cancer survivors, with 150' per week of moderate-intensity aerobic exercise, 2 to 3 days of resistance training, and large muscles flexibility training. The constant use of these muscle in daily routines may also have helped these results. Like us, no significant improvement was found in BMI. The length of the program, or the fact that no nutritional support was given, might justify the lack of BMI improvements.

Our findings that are related to lower limb strength, are in agreement with the literature, with concerning intervention effects. Galiano-Castillo et al. (2016), in a homebased, supervised, tailored combined exercise intervention of 8 weeks, with social component associated through text messages, questions, suggestions (post training), and videoconferences or phone calls (3 times per week), based on ACSM's Guidelines for cancer survivors, also observed significant improvements in lower limb strength. In the study of Dong et al. (2020) they observed, like us in the On4Rehab protocol, significantly improves in lower limb strength. Their assessment was made one year after completing the program. The intervention was like ours, with remote supervision of combined training (4 days of aerobic training and 3 days of resistance training) but in this case for 12 weeks. It may be interesting to see if after an 8-week intervention, the results are also like Dong and colleagues' (2020). Ariza-Garcia et al. (2019) with a web based combined exercise intervention (5 strength exercises and 15-30' aerobic exercises of moderate-intensity) of 8-week length, also observed lower limb strength significantly improves.

The significant improvement in the hip circumference in the CB group can be related to the baseline values of the participants. According with the principle of initial values, improvements in the outcome of interest will be greatest in those with lower initial values (Bland et al., 2021). In this group, the average values of the hip circumference at baseline, were much higher than the observed values in the HB group. Ariza-Garcia et al. (2019) didn't find improvements in anthropometric values in their study, despite having a web based combined exercise intervention (5 strength exercises and 15-30' aerobic exercises of moderate-intensity) of 8-week length, delivered to a group of 68 participants who were undergoing chemotherapy. The fact that the On4rehab protocol has greater volume (duration of aerobic training and number of strength exercises) and intensity (moderate to vigorous) may help explain this difference associated to the fact that our participants were not

undergoing chemotherapy anymore, which in itself can be a factor for reduced capacity for training.

No correlation between the percentage of adherence to the sessions and any change of the variables was found neither in all the sample nor in each group in separate. no study was found in the literature that compares this relationship and thus allows us to compare our findings.

Limitations

The recruitment only took place in CHVNG/E can be pointed as a limitation. Recruitment may have taken longer for this reason. The fact that assistant oncologists defend this type of intervention may also have positively influenced the decision of the participants.

The sample size, despite being a pilot study, makes the analyzes to be considered preliminary, thus needing to apply the protocol to a larger sample, to check what was verified.

Because there is a homebased format, elastic bands were the only accessory material to strength training. In this way, the control of the training intensity could not be so efficient as it would be in a weight training machine where it is possible to gradually increase the resistance (load) to keep the participants within the desirable RPE. The data reporting the intensity of aerobic training (RPE) in the CB group was not consistent, so no analysis was made to this variable.

Despite the recommendations given (time and number of steps) for the third weekly training session (aerobic), this was not supervised. Thus, the lack of supervision may have affected the intensity at which the participants performed this training. Also, the fact that there is some illiteracy in the use of the "Pedometer" application meant that the feedbacks from that training session sometimes did not reach physiologists in the most correct way.

Conclusion

In conclusion, this pilot study gave interesting findings regarding the On4Rehab intervention and suggests that it could be safe and feasible to deliver the program to breast cancer survivors. We found that the On4Rehab protocol may improve upper limb strength, lower limb strength, and waist circumference. The results also indicate that the On4Rehab protocol is well accepted by the participants. The high retention and adherence rates and the fact that

there are no significant differences between groups suggest that the application of the program in a supervised HB version is feasible and similar in terms of effectiveness to the CB version. Adherence report and transparency is needed to continue to improve exercise interventions design and continue to improve the interventions to these patients.

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