A-CaRe study 1. Exercise after chemotherapy.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22359

Source
Nationaal Trial Register

Brief title
REACT

Health condition

cancer survivors, physical exercise, chemotherapy, fatigue, physical fitness, quality of life, training, strength,

Sponsors and support

Primary sponsor: EMGO Institute for Health and Care Research, VU medical Center
Maxima Medical Center
Source(s) of monetary or material Support: Stichting Alpe d'HuZes / KWF kankerbestrijding

Intervention

Outcome measures

Primary outcome

1. Cardiorespiratory fitness;

2. Muscle strength;

3. Fatigue.

Ad1. Cardiorespiratory fitness is measured during a maximal exercise test on an electronically braked cycle ergometer according to a ramp protocol in which the resistance gradually increases every 6 seconds aiming to achieve a maximum within 8 to 12 minutes. Patients are instructed to cycle with a pedal frequency between 70 and 80 rpm, and are encouraged to continue exercising until exhaustion or inability to maintain the pedal frequency of 70 rpm. Expired gases are collected and analyzed breath by breath for O2, CO2, and volume. The average values of the last 30s of exercise are used as measure for peak oxygen consumption (peakVO2), peak power output, and peak heart rate.

Ad2. Upper extremity muscle strength of adults is measured using a JAMAR grip strength dynamometer. Lower extremity muscle strength is tested by the functional 30s chair stand test, according to a standardized measurement protocol.

Ad3. Two self-report questionnaires are used to assess fatigue: the Multidimensional Fatigue Inventory (MFI) and the Fatigue Quality List (FQL). The MFI consists of five subscales based on different dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. THE FQL consists of four subscales: frustrating, exhausting, pleasant, and frightening.

Secondary outcome

1. Body composition;

2. Health-Related Quality of Life;

3. Self-reported physical activity;

4. Mood disturbance;

5. Functioning in daily life;

6. Return to work.

Ad1. Body height, body weight, waist and hip circumferences, and four skinfolds (biceps, triceps, suprailiac and subscapular) are assessed to estimate body composition. In addition, a

dual-energy x-ray (DEXA) scan will be performed.

Ad2. The European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire C30 (EORTC QLQ-C30) is a questionnaire developed to assess the health-related quality of life of cancer patients. The EORTC QLQ-C30 encompasses 30 items divided in five functional scales (physical, role, emotional, cognitive, social), three symptom scales (pain, fatigue, and emesis) and an overall QoL scale. Additional single items address other symptoms commonly experienced by cancer patients (e.g., insomnia, diarrhea, constipation, etc.).

Ad3. To assess self-reported levels of physical activity, we will either use the Physical Activity Scale for Elderly (PASE) or the Activity Questionnaire for Adults and Adolescents (AQuAA), depending on the most valid and reliable questionnaire in cancer patients. At the moment, we are conducting a study to determine which of the two questionnaires had the best psychometric properties.

Ad4. Mood disturbance will be assessed with the 14-item Hospital Anxiety and Depression Scale (HADS). The HADS assesses symptoms of mood disturbance, yielding separate scale scores for anxiety and depression, as well as a total score.

Ad5. Functioning in daily life will be assessed with the Impact on Participation and Autonomy (IPA) Questionnaire.64 The IPA Questionnaire consists of 32 items assessing perceived level of participation and autonomy, organized into 5 domains: autonomy in the home, family role, autonomy outside of the home, social relations, and work and education. An additional 9 items assess perceived problems with participation and autonomy.

Ad6. The following indicators of return to work will be measured: 1) Time to partial and to full RTW, meaning number of calendar days between end of treatment and first day at work; 2) Time to full RTW corrected for partial RTW; 3) Partial and full RTW rate at 12, 18 and 70 weeks follow-up. All will be assessed by self-report.

Other study outcomes:

1. Compliance: Compliance with the physical activity and exercise programs will be assessed by self-report and exercise logs filled in by physiotherapists after every training session (e.g.,

observed attendance at and compliance with the exercise protocol);

2. Satisfaction with the intervention: Satisfaction with the intervention will be assessed, only at T1. Patients in the two intervention arms are asked to complete a series of questions about the perceived efficacy of and satisfaction with the program, whether they would suggest any changes to the program, and if they would recommend it to other patients undergoing chemotherapy. This questionnaire will be administered at the end to prevent biasing the other questions. Perceived efficacy and satisfaction will either be rated on a Visual Analogue Scale or on a 7-level Likert type scale. Both measures are considered valid and reliable;

3. Sociodemographic and clinical data: Sociodemographic data such as age, education, marital status, living situation, work status, weight and length, medication use (including alternative medications or therapies) and lifestyle variables (e.g. smoking, physical activity and exercise levels prior to diagnosis) will be obtained via a questionnaire. Clinical information, including date of diagnosis, stage and subtype of disease, and treatment history will be obtained from the medical records. During the follow-up period data on disease status (response to treatment, progression or relapse) and data on any additional treatment will be collected;

4. Moderating variables: A series of questions will be posed at baseline to assess a number of potential moderating variables, and variable that may be predictive of compliance with the physical exercise programs. These will include pre-illness lifestyle (frequency, nature and intensity of physical activity and exercise behavior, or avoidance thereof), current attitudes towards and beliefs about exercise, in general, and exercising after chemotherapy, in particular. Information about behavioural beliefs, normative beliefs, control beliefs, attitude, subjective norm, perceived behavioural control, and intention will be collected using standardized questions as described by Courneya and colleagues. These questions have been used to evaluate exercise programs in cancer survivors and are based on established health behaviour theories, in particular the Theory of Planned Behaviour.

Study description

Background summary

Background:

Physical exercise has been identified as a potential intervention to improve physical fitness, fatigue and health-related quality of life in cancer patients after chemotherapy. From available systematic reviews it is concluded that additional exercise intervention studies are needed to more firmly establish the range and magnitude of positive effects of physical activity among cancer survivors.

Purpose:

The proposed study is part of a larger KWF program proposal: the Alpe d'HuZes Cancer Rehabilitation Research Program ('A-CaRe') coordinated by the EMGO Institute in Amsterdam. A-CaRe study 1 aims to evaluate the effectiveness and cost-effectiveness of a high-intensity resistance and interval exercise program in cancer survivors after chemotherapy. The high intensity program will be compared to a moderate intensity program mostly focused on aerobic exercise and leisure sports and a waiting list control group.

Plan of investigation:

This is a randomised controlled trial. After baseline measurements, subjects will be randomly assigned to the following 3 groups:

1. 12 weeks twice weekly high intensity strength and aerobic interval training (n=140) in groups of 5 to 8 participants directed by a trained physical therapist. The resistance program consists of six exercises targeting six large upper and lower extremity muscle groups. Resistance exercises are performed at 65% to 80% of one-repetition maximum (1-RM) and consist of two sets of 10 repetitions. The interval training consists of cycling two times eight minutes, before and after the resistance exercises, with work load alternating between 30 and 65% of the maximum work load;

2. 12 weeks twice weekly the 'Herstel and Balans' program (n=140) with exercises mostly focused on aerobic exercise and leisure sports. 'Herstel and Balans' is currently available as usual care in the Netherlands;

3. A waiting list control group (n=120) who receives the high intensity program or 'Herstel and Balans' program 12 weeks after baseline and randomisation.

Measurements are performed at baseline (T0), after 12 weeks (T1), and 1 year after completing the completing the intervention (T2).

The primary outcomes are cardiorespiratory fitness and muscle strength assessed by objective performance indicators, and self-reported fatigue. Secondary outcomes include self-reported physical activity and physical functioning, mood state, return to work and health-related quality of life. Additionally, compliance and satisfaction with the interventions are evaluated. Potential moderating variables, including pre- and post-illness lifestyle, and health- and exercise-related attitudes, beliefs and motivation, will also be assessed. In addition, the cost-effectiveness of the high intensity strength training will be evaluated.

Relevance:

This project will make a significant contribution towards the implementation of evidence

based cancer rehabilitation programs.

Study objective

1. Cancer survivors who received the high-intensity exercise program will have significantly higher muscle strength, cardiopulmonary function, and health-related quality of life after 12 weeks intervention compared to cancer survivors who received the 'Herstel and Balans' program or waiting list control;

2. Cancer survivors who received the high-intensity exercise program will have significantly reduced fatigue after 12 weeks intervention, compared to cancer survivors who received current standard of care (Herstel and Balans or waiting list control);

3. Cancer survivors who received the Herstel and Balans program will have significantly higher muscle strength, cardiopulmonary function, and health-related quality of life after 12 weeks intervention compared to cancer survivors assigned to waiting list;

4. Cancer survivors who received the Herstel and Balans program will have significantly reduced fatigue after 12 weeks intervention, compared cancer survivors assigned to waiting list;

5. The changes in physical fitness will mediate, in part, the beneficial effect of exercise on fatigue and health-related quality of life;

6. One year after completing the rehabilitation program, the high intensity exercise group will will have significantly higher muscle strength, cardiopulmonary function, and health-related quality of life compared to the group that received the Herstel and Balans program;

7. One year after completing the rehabilitation program, the high intensity exercise group will will have significantly reduced fatigue compared to the Herstel and Balans group);

8. Cancer survivors who received the individualized high-intensity exercise program will return to work significantly sooner than cancer survivors who received current Herstel and Balans program;

9. The high-intensity exercise program is more cost-effective compared to current standard of care (Herstel and Balans or waiting list control).

Study design

T0: baseline measurement, prior to randomization;

T1: at completion of the 12-week intervention;

T2: 12 months after ending the intervention.

Intervention

1. High-intensity strength and endurance training;

2. Herstel & Balans program;

3. Waiting list control.

Ad1. High intensity strength and endurance training.

The 12-week training program consists of high-intensity strength and endurance training. The safety of the program is guaranteed by a comprehensive intake procedure that will guide the training. Before the start of the program, each patient's cardiopulmonary and muscular limitations are determined by consultation with a sports physician and by a VO2 max test. If necessary, adaptations in training methods or specific advise to patient and physiotherapists is given, using this information. The patients train in groups of 6-8 persons on specialized resistance training equipment and bicycle ergometers. The patients train twice a week under supervision of a physiotherapist.

The resistance program consists of six exercises targeting the large muscle groups as follows: 1) vertical row; 2) leg press; 3) bench press; 4) pull over; 5) abdominal crunch; 6) lunge. Resistance exercises are performed at 65% to 80% of one-repetition maximum (1-RM) and consist of two sets of 10 repetitions. Every four weeks the training progress is evaluated, and the result is adjusted by means of a 1-RM test.

The endurance training consists of cycling two times eight minutes, before and after the resistance exercises, with work load alternating between 30 and 65% of the maximal short exercise capacity (MSEC) assessed by the steep ramp test. Every four weeks the training progress is evaluated, and the result is adjusted by means of the steep ramp test. The steep ramp test - an incremental bicycle ergometer test – has proved to be a convenient alternative in cancer survivors to determine training dose, and reliable (ICC = 0.996) and valid (correlation with VO2max of 0.85) test to estimate maximal workload in cancer patients. Subjects are instructed to cycle at a speed between 70 and 80 RPM, starting at 25W, after which the load is increased by 25 Watts every 10 seconds. The test ends if cycling speed falls below 60 RPM. Maximal workload, time cycled at that load and heart rate at the end of the test are recorded.

Ad2. 'Herstel and Balans' program.

The 'Herstel and Balans' program is based on a bio-psychosocial approach. The program takes 12 weeks, during which groups of 12-16 participants visit the rehabilitation centre for group-based physical rehabilitation and psycho-education. The physical rehabilitation is

based on the graded activity theory and consists of supervised sessions, twice a week and is being offered at more than 50 locations in the Netherlands. All patients receive the same intervention including training at a light to moderate intensity level. Heart-rate monitors will be used to ensure that the participants train at the correct intensity. The training consists mainly of endurance training, some moderate endurance strength training, some types of ball sports and breathing exercises. The training can differ between institutions but in general will be mostly focused on aerobic exercise and leisure sports rather than on high intensity strength training. Since all patients are enrolled through the same hospital and the 'Herstel and Balans' program is conducted in one centre (Blixembosch) we are able to standardise the 'Herstel and Balans' program in this trial. This centre has experience with this program since more than 4 years.

After 12 weeks of supervised training, both interventions will include three booster sessions: at 4, 10, and 18 weeks after T1. These booster sessions will be in line with respective interventions, and consist of training and counselling by the treating physician or physical therapist to motivate patients to continue exercising and to maintain a physically active lifestyle in general. The advise will be tailored to the individual patient based on personal restrictions and needs, attitudes, perceived barriers and other determinants of physical activity. These face-to-face sessions will be supported by folders about the Dutch physical activity guidelines.

Ad3. Patients from the waiting list control group are offered the high intensity exercise or 'Herstel and Balans' program 12 weeks after baseline measurements. Because a waiting list control group may be problematical in a region were oncological rehabilitation programs are offered, we plan the following procedure: we will explain to all eligible patients that they will be randomly assigned to high intensity training or 'Herstel and Balans'. Next participants in these groups will be randomly assigned to an immediate start of the training or to waiting list. In real life there is currently also a waiting list for the 'Herstel and Balans' program. Also in the current guidelines of 'Herstel and Balans' it is a rule to start not before 3 months after finishing treatment. As a consequence of randomizing this group to one of the 2 interventions, the long-term follow-up will be a follow-up of the respective intervention.

Contacts

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Eligibility criteria

Inclusion criteria

1. Histological confirmed breast, colon, ovarian cancer or lymphomas with no indication of recurrent or progressive disease;

2. Age between 20 and 70 years;

3. Completion of (adjuvant) chemotherapy with curative intention and completion of surgival treatment or radiotherapy.

Exclusion criteria

1. Wheelchair dependent, or not able to perform basic activities like walking or cycling;

2. Contraindications for phsycial activity or exercise;

3. Serious psychiatric or cognitive problems or severe emotional instability;

4. Malnutrition;

5. Not familiar with the Dutch language;

6. Unable to follow exercise instructions;

7. Participating in concurrent studies or rehabilitation programs containing physical activity or exercise.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2010
Enrollment:	400
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL2036
NTR-old	NTR2153

Register	ID
Other	KWF : ALPE 2009-4619
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A