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A trial to detect differences in arm volume after heavy and low load resistance exercise among patients receiving adjuvant chemotherapy for breast cancer at risk for arm lymphedema

Submission date
21/01/2015

Recruitment status
No longer recruiting

Registration date
12/02/2015

Overall study status
Completed

Last Edited
19/10/2017

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Women who have had breast cancer treatment may be at risk of a condition called lymphedema. During surgery, one or more lymph nodes from under the arm may be removed to see whether the cancer has spread from the breast to other areas. This involves removing lymph vessels that carry lymph fluid from the arm to the rest of the body. This results in changes to the flow of this lymph fluid and may result in a build-up of fluid, causing swelling, or lymphedema. Breast cancer-related arm lymphedema (BCRL) is increasingly becoming a public health concern. Resistance training (or weight training) with low to moderate loads (weights) has been found to be safe and beneficial, resulting in increased strength and function of the limb. RT is also likely to help the clearance of lymph through the effect of the muscle working. However, results from exercise science studies suggest that heavy load RT may be more beneficial with heavier loads being associated with larger gains in function and quality of life. Despite these benefits, health professionals advise patients to avoid heavy lifting as it is assumed to increase the risk of BCRL. However, this assumption is not based on research. Furthermore, uncertainty exists regarding the best time to start RT in the time after a cancer diagnosis. The purpose of this study is to explore whether there is a difference in arm volume after RT with low loads compared to heavy loads among patients receiving adjuvant chemotherapy for breast cancer.

Who can participate?
Patients with breast cancer will be found from a waiting list to “Body and Cancer”, a 6 week exercise program offered to cancer patients receiving chemotherapy in the Copenhagen area. To be included in this study, patients must be over 18 years of age, have undergone surgery on one breast, have had associated lymph nodes removed and are currently receiving standard adjuvant chemotherapy.

What does the study involve?
Participants are recruited before their third chemotherapy treatment. They are asked to maintain normal daily- and physical activity levels throughout the study, and not to do any RT.

During week three of their third chemotherapy cycle, all participants are asked to take part in a familiarization period. This involves two RT sessions during the week. Each of these two sessions start with a 10 minute warm up on a cross-trainer. During the first familiarization session participants are introduced to- and strength tested in four arm exercises in order to make individually prescribed RT programs. During the second familiarization session participants will strength train using the four RT exercises and a new strength test will be carried out to ensure accuracy. After their fourth chemotherapy treatment, participants are asked to take part in two experimental RT exercise sessions - one involving low load exercises and the other heavy load. Participants are randomly assigned to participate in either the low or heavy load experimental exercise session first. The first experimental session takes place during week two after the fourth chemotherapy treatment followed by a period of at least three days before the fifth chemotherapy treatment. Participants have arm volume measured before, immediately after and 24- and 72 hours after each experimental session. All measurements are performed at the Clinical Nuclear and Physiological Department, Rigshospitalet.

What are the possible benefits and risks of participating?
As this intervention includes exercise there is always the risk of sports related injuries. However, as training sessions will be performed in a controlled setting with individual attention, the risk of injury is considered very low. As 20-30% of women treated for breast cancer develop BCRL it is expected that some of the participants in this study will develop BCRL. However, based on previous research, we believe that participation in this study does not pose an additional risk. Furthermore, because the participants will be assessed for BCRL using the best technology to date, early detection of BCRL is possible. If a participant develops signs of BCRL lasting over one week during the study period, they will be referred to hospital lymphedema therapists for evaluation and treatment and will not be allowed to continue in the study.

Where is the study run from?
All sessions are performed at training facilities located at Rigshospitalet.

When is the study starting and how long is it expected to run for?
June 2014 to October 2016

Who is funding the study?
University Hospitals Centre for Health Research (UCSF) (Denmark)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Low and heavy load resistance exercise: acute response on arm volume among patients receiving adjuvant chemotherapy for breast cancer at risk for arm lymphedema

Study objectives
Based on previous studies finding upper body resistance training (RT) with low and moderate loads to be a safe training modality, and in line with Cormie et al. (2013) it is hypothesized that:
1. No differences in extracellular fluid or volume of the “at risk” arm will be observed over time (pre- and post exercise, 24- and 72 hours post exercise) in both low and heavy load RT.
2. No differences in extracellular fluid or volume will be observed between limbs in both RT sessions across time points.
3. No increases in symptom severity will be observed in both RT sessions and no differences in symptom severity will be observed between RT sessions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethical committee of the Capital Region, Copenhagen, Denmark, 06/01/2015, ref: H-3-2014-147
2. The Danish Data Protection Agency, 16/01/2015, ref: 30-1430

Study design
Two-armed randomized cross-over trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Patients receiving adjuvant chemotherapy who are at risk of developing breast cancer related arm lymphedema

Interventions

After obtainment of signed consent and screening for breast cancer related arm lymphoma, participants will be randomized with an allocation of a 1:1 ratio to partake in either the heavy or low load experimental exercise session first.

Exercise sessions
Participants will be recruited prior to their first docetaxel treatment and will engage in a familiarization period during week three of their third cycle. The familiarization period will comprise of 2 training sessions during the course of one week. Each session will start with a 10 minute warm-up on a cross-trainer (Technogym®, Gamettola, Italy). During the first familiarization session participants will be introduced to the four upper extremity exercises (chest press, latissimus pull down, triceps extension) (Technogym®, Gamettola, Italy) and biceps curl with free weights followed by a 1RM strength test to determine individually prescribed RT programs. During the second familiarization session 2 sets of 10-15 RM will be performed in the four exercises and a new 1RM strength test will be performed to ensure accuracy.

Participants will engage in the first experimental session during week two after the first docetaxel series followed by a wash-out period of at least three days and prior to the second docetaxel series. Participants will engage in 3 sets of 5-8 RM of each exercise during the heavy load experimental session, where as 2 sets of 15-20 RM will be performed in the low load experimental sessions. All sessions will be performed at our training facilities located at Rigshospitalet in individual training sessions supervised by a physical therapist/ or exercise physiologist.

Intervention Type
Behavioural

Primary outcome(s)
Current primary outcome measures as of 16/10/2017:
Extracellular fluid (L-Dex) is measured using Bioimpedance spectroscopoy at pre-exercise, post-exercise, 24 hrs post-exercise, 72 hrs post-exercise

Previous primary outcome measures:
1. Measurement outcomes will be recorded just prior to and after the experimental RT sessions, and again after 24 and 72 hours and will be performed with no knowledge of exercise allocation at the Clinical Nuclear and Physiological Department, Rigshospitalet.
2. Extracellular fluid: BIS directly measures extracellular fluid and therefore has a high reliability for detecting BCRL development as it initially is characterized by an excess of extracellular fluid. BIS will be applied to measure the impedance of extracellular fluid for each limb at a range of frequencies assessed using the manufacturer's software (SFB7, Impedimed, Brisbane, Australia). The ratio of impedance values between the limb at risk and non-affected limbs, will be calculated and converted into a lymphedema index (L-Dex) score. An increase in a L-Dex score denotes an increase in extracellular fluid.

Key secondary outcome(s))
Current secondary outcome measures as of 16/10/2017:
1. Inter-arm volume difference (%) is measured using Dual X-ray absorptiometry at pre-exercise, post- exercise, 24 hrs post-exercise, 72 hrs post-exercise
2. Breast cancer-related symptoms (heaviness, swelling, tightness, pain) is measured using a numeric rating scale (0 (no discomfort) -10 (severe discomfort)) at pre-exercise, post- exercise, 24 hrs post-exercise, 72 hrs post-exercise

Previous secondary outcome measures:
1. Arm volume: DXA (Lunar Prodigy Advanced scanner, GE Healthcare, Madison, WI,) assesses tissue composition (lean mass, bone mineral content, fat mass) of the limbs using a three compartment model that is sensitive to changes in upper limb tissue composition and upper limb volume and is considered safe and easy to perform. Subjects will be positioned on the scan table lying supine and with the arm separated from the trunk. Each arm will be scanned. Software version (Small animal program version 8.1027) will be used to analyze the scans. Using previously derived densities for: fat (0.9 gm/ml); lean mass (1.1gm/ml); bone mineral 1.85 gm /ml), the measured DXA tissue weights will be transformed into estimated volumes using the following equation: v=m/d where v=volume and d=density.
2. Subjective assessment of symptoms: Symptom response to the training bouts will be monitored using the visual analogue scale (VAS). VAS will be used to quantify the severity of perceived swelling, heaviness, pain and tightness in both the non-affected limb and the limb at risk. Participants will rate their symptom severity from no discomfort (VAS=0) to very severe /worst imaginable discomfort (VAS=10).

Completion date
01/10/2016

Eligibility

Key inclusion criteria
A convenience sample of patients with breast cancer will be identified from a waiting list to “Body and Cancer”, a six week exercise program for cancer patients in chemotherapy in the Copenhagen area. Patients are eligible for “Body and Cancer” if they have a diagnosis of cancer, have received at least one cycle of chemotherapy for advanced disease or as adjuvant treatment, have a WHO performance status of 0 or 1 and otherwise have been approved to participate by the treating oncologist. Eligible participants will be invited to be screened for BCRL using BIS and DXA and will be inspected for signs of swelling by the applicant. An L-Dex score of 10 or greater, or a volume difference between the affected and non-affected limb of 5% or more; swelling or obscuration of anatomic architecture on close inspection; pitting edema, will be defined as BCRL according to CTC v3.0 Lymphedema Criteria.

Inclusion criteria:
1. Patients over 18 years of age who have undergone unilateral breast surgery for breast cancer (stage l-lll) with AND beyond the sentinel node
2. Currently receiving standard adjuvant chemotherapy

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

Female

Key exclusion criteria
1. A diagnosis of BCRL as defined above
2. Currently receiving treatment for lymphedema
3. Conditions hampering RT of the upper extremities
4. Previous treatment for breast cancer
5. Participated in regular RT (2x/week) of the upper extremities during the last month

Date of first enrolment
26/01/2015

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
Denmark

Study participating centre
The University Hospitals Centre for Health Research
Copenhagen University Hospital (Rigshospitalet)
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Sponsor information

Organisation
University Hospitals Centre for Health Research (Denmark)

ROR
https://ror.org/04n8nb568

Funder(s)

Funder type
Hospital/treatment centre

Funder Name

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Kira Bloomquist at kira.bloomquist@regionh.dk until January 2022. Anonomyzed data will be made available for systematic review or to researchers in the field. Outcomes include L-Dex, interarm volume and lymphedema symptom severity rated on a 0-10 scale. Consent from all participants were obtained.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	22/07/2016		Yes	No
Basic results		04/10/2017	19/10/2017	No	No