The impact of caloric restriction versus exercise on tumor and muscle tissue protein synthesis rates in breast cancer patients

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To determine the the impact of 30% daily caloric restriction or daily exercise training on tumor and muscle tissue protein synthesis rates in breast cancer patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON56422

Source
ToetsingOnline

Brief title
CREX Study

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer, muscle

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Breast cancer, Energy intake, Exercise, Skeletal muscle

Outcome measures

Primary outcome

1. Tumor tissue protein synthesis rates over the 7-day intervention period in

breast cancer patients.

2. Muscle tissue protein synthesis rates over the 7-day intervention period in

breast cancer patients.

Secondary outcome

Healthy breast tissue protein synthesis rates over the 7-day intervention

period. Plasma concentrations of estrogen, insulin, growth hormone, IGF-1,

IGFBP-1, IGFBP-3, C-reactive protein, IL-1, IL-6, TNF-alpha, IL-10.

Study description

Background summary

Cancer is among the most prevalent diseases worldwide, with predictions that 15 million cases will be diagnosed and 10 million new cancer-related deaths will occur next year. Despite recent improvements in treatment success rates, there remains substantial opportunity to further enhance the efficacy of cancer treatment to reduce tumor growth. Tumor growth is regulated by the net difference between tumor tissue protein synthesis and breakdown rates. Several factors regulate tumor protein synthesis, including circulating anabolic hormones (i.e., IGF-1). Reducing the presence of these factors has been suggested to reduce cancer incidence and lower tumor tissue growth rates. Cancer progression and standard treatment are often accompanied by adverse side effects, such as fatigue and skeletal muscle mass loss, termed cachexia, which worsens treatment outcomes. Lifestyle modifications, such as diet and physical activity interventions, represent promising adjunct therapeutic approaches that may induce anti-carcinogenic effects while reducing fatigue and skeletal muscle loss. Moderate caloric restriction and exercise are two promising intervention

strategies that may impact tumor tissue protein synthesis rates.

Study objective

To determine the the impact of 30% daily caloric restriction or daily exercise training on tumor and muscle tissue protein synthesis rates in breast cancer patients.

Study design

Subjects will be randomly assigned to undergo 7 days of either caloric restriction, an exercise program, or standard treatment. The caloric restriction group will undergo a 30% reduction in daily energy intake (~500-600 kcal). The exercise group will increase daily energy expenditure by 30% (~500-600 kcal) by performing 1 h of combined resistance- and endurance-type exercise and 30 min of walking. Patients following standard treatment will act as the control group. All subjects will ingest small amounts of deuterium oxide (2H2O) throughout the 7-day period. The 7-day period will end with the tumor resection surgery, during which a tumor tissue sample, skeletal muscle sample, and plasma sample will be collected. Protein will be isolated from the tissue samples and analyzed for the increase in 2H-alanine enrichment to determine average tumor and muscle tissue protein synthesis rates over the 7-day assessment period (in %/d).

Intervention

Caloric restriction:
The caloric restriction group will be subjected to a 30% reduction in daily dietary energy intake (500-600 kcal per day) while maintaining the same relative macronutrient intake (i.e., 15/55/30% Pro/CHO/Fat) over the 7-day intervention period. A nutritional program will be generated for each patient, with total energy based on usual energy intake assessed with a dietary history with cross-check. During the intervention, subjects will receive standardized meals and will receive individualized dietary consultation from the researcher in collaboration with the Department of Dietetics to ensure compliance and avoid malnutrition.

Exercise:
The physical activity group will increase daily energy expenditure by 30% (500-600 kcal) by performing 1 h of combined resistance- and endurance-type exercise and 30 min walking. Participants in the physical activity group will perform the exercise protocol (either at MUMC+ or at home) under the supervision of a certified personal trainer. The endurance-type exercise component will consist of 30 min cycling at 70% estimated maximal heart rate (estimated maximal heart rate = 220-Age). The resistance-type exercise component will consist of 3 sets each of leg press (or dumbbell squats), leg

extension (or dumbbell lunges), chest press, and horizontal row performed at 70% of 1-RM or for 8-12 repetitions per set. Subjects will be instructed to carry-out 30 min of walking (e.g., 2 x 15 min) at home each day in addition to habitual physical activity.

Control:
The control group will follow standard treatment and not under caloric restriction or exercise.

Study burden and risks

The burden and risks involved in participating in this experiment are small. The tumor and healthy breast tissue collection will occur during the tumor resection procedure (lumpectomy), which will already be planned as part of the subjects* course of cancer treatment. Muscle biopsies will be obtained during the surgery under anaesthesia by an experienced physician, but may cause some minor discomfort. The discomfort is comparable to muscle soreness or the pain one has after bumping into the corner of a table. Isotopically-labelled water (deuterium oxide or *heavy water*) ingestion has been used previously in numerous published studies and is entirely safe and non-toxic in the amount provided in the present study. We have chosen to include breast cancer patients not undergoing chemo or radiotherapy as they are generally non-frail and will be able to tolerate caloric restriction or daily exercise. Caloric restriction of 30% lower than habitual dietary intake is commonly prescribed as a weight management strategy and will not lead to adverse effects (e.g., dizziness) or compromise preparation for the lumpectomy procedure. Daily exercise (1 h) is well-tolerated by patients, but participants may experience muscle soreness induced by unaccustomed exercise.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1) Female
2) BMI 18.5-35.0 kg/m2
3) Diagnosed with breast cancer, with treatment requiring a lumpectomy

Exclusion criteria

1) Patients receiving preoperative chemo- or radio-therapy
2) >5% weight loss in the previous 6 months
3) Fasting glucose >7 mmol/L
4) Musculoskeletal injuries (which may interfere with performing the exercise program)
5) Participation in structured resistance exercise program
6) A history of neuromuscular problems
7) Use of anti-coagulants
8) Use of protein and/or fish-oil supplements
9) Participation in a 2H2O study in the previous 6 months

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-05-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	05-08-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	18-11-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL74121.068.20
Other	This study will be registered following approval from the METC