The impact of 18 weeks of chemotherapy-treatment with Taxotere/Adriamycin/Cyclophosphamide (TAC) on skeletal muscle composition of female breast cancer patients

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The aim of this study is to define the specific changes in skeletal muscle composition and function, systemic inflammation and nutritional intake and physical activity levels, during cancer treatment. To investigate this, we will include 13 female...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON37832

Source
ToetsingOnline

Brief title
Impact of chemotherapy on muscle composition of breast cancer patients

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
cachexia, loss of muscle mass

Research involving
Human

Sponsors and support

Primary sponsor: Maxima Medisch Centrum
Source(s) of monetary or material Support: Stichting Stimulering Onderzoek Sport en Bewegen bij Kanker

Intervention

Keyword: cachexia, cancer, inflammation, muscle strength

Outcome measures

Primary outcome

The primary objective of this study is to investigate the impact of 18 weeks of chemotherapy-treatment on markers of skeletal muscle composition (muscle fiber type distribution and cross sectional area, muscle fiber glycogen and fat concentration, muscle fiber capillarization, muscle fiber satellite cell content), and metabolism (muscle citrate synthase, cytochrome c oxidase, succinate dehydrogenase and beta-hydroxyacyl-CoA dehydrogenase activity). These markers will be measured in skeletal muscle biopsies from 13 female breast cancer patients taken from the vastus lateralis muscle before and after chemotherapy.

Secondary outcome

Secondary objectives of this study are to investigate the impact of 18 weeks of chemotherapy-treatment on:

- Body composition (body weight, length, fat mass, muscle mass and bone density): measured by DEXA, BMI, hip and waist circumference and body fat percentage, before and after chemotherapy
- Aerobic capacity (maximal oxygen uptake capacity): measured by a maximal cycling test with respiratory gas analysis, before and after chemotherapy

- Muscle strength: measured by a one repetition maximum strength test (1-RM) on the leg-extension and leg-press machine, before and after chemotherapy

- Metabolic and inflammatory profile (haemoglobin, haematocrit, C-reactive protein, leucocytes, glucose, insulin, free fatty acids, creatinine, myoglobin, insulin-like growth factor 1, tumor necrosis factor alpha and its receptor, interleukins 1 and 6, interferon gamma, cortisol, testosterone): measured by venous blood sampling, before and after chemotherapy.

- Physical activity level, dietary status, level of fatigue, and quality of life: measured by different questionnaires, before and after chemotherapy.

Study description

Background summary

Recent population demographics of the Netherlands show that an increasing number of people are diagnosed with cancer each year. In 2007 86.800 people were diagnosed with cancer, and this number is expected to increase to 123.000 in 2020. This progression is a result of the growing number of people aged 65 years and over, together with a general aging of the population. Fortunately, during the past few decades, the detection and treatment of cancer has made substantial progress, leading to improved survival. The 5-year survival in male cancer patients has increased from 41% in 1993 to 54% in 2007, and similar increases are reported for female patients. Consequently, by 2020 the number of cancer survivors in the Netherlands will be ~666.000, which represents ~4% of the entire population. As both the number of cancer survivors and the length of their survival increases, long-term health issues related to cancer and its treatment are becoming more important.
A very serious side effect of cancer and its treatment concerns cachexia. Cancer cachexia is defined as a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. It is associated with reduced physical function, reduced tolerance to anticancer therapy, and reduced survival. Furthermore, loss of skeletal muscle mass is accompanied by an increased risk of developing chronic metabolic diseases like obesity and type 2 diabetes.
To counteract these catabolic effects of cancer and its treatment, it is

important to identify the specific changes that occur in skeletal muscle composition and function during cancer treatment. Research on skeletal muscle composition during cancer treatment is very limited. Previous studies have shown that cancer patients have lower endurance capacity and muscle strength compared with healthy controls, and that this is accompanied by a decrease in muscle fiber size and an increase in intramyocellular lipid content. However, in order to get more insight into the pathophysiology of cancer cachexia, it is important to study the specific changes in skeletal muscle tissue of cancer patients that occur during treatment, and moreover to investigate these changes in much more detail than described previously.

Study objective

The aim of this study is to define the specific changes in skeletal muscle composition and function, systemic inflammation and nutritional intake and physical activity levels, during cancer treatment. To investigate this, we will include 13 female breast cancer patients and assess body composition, skeletal muscle composition, strength, and endurance capacity before and after 18 weeks of chemotherapy. In addition we will measure markers of metabolism and systemic inflammation in venous blood samples and determine changes in nutritional intake and physical activity with different questionnaires.

Study design

The study is designed as an observational trial, comparing skeletal muscle characteristics, body composition, aerobic capacity, muscle strength, metabolic and inflammatory profile, and physical activity, diet and quality of life in patients with breast cancer before and immediately after 18 weeks of chemotherapy-treatment. An overview of the study design is shown in Figure 1 at page 8 of the research protocol. Patients will be selected for participation by their surgeon and oncologist in the period between surgery and start of chemotherapy-treatment (usually 4 weeks). After informed consent is obtained, the baseline tests will be performed on 2 separate occasions. The first tests (T1) will be conducted 2 weeks before the start of chemotherapy at Máxima Medical Centre Veldhoven, consisting of measurements of body composition, maximal cycling exercise with respiratory gas analysis, and a muscle strength assessment. The second part of testing (T2) will be conducted 1 week later at Máxima Medical Centre Veldhoven, and includes a muscle biopsy from the vastus lateralis muscle, blood sampling from an antecubital vein, filling out the questionnaires under supervision of the researcher, and a muscle strength confirmation test. Questionnaires will be repeated by mail in the week before the 4th chemotherapy session (Q). After 18 weeks of chemotherapy-treatment all subjects will undergo the same tests again (T1 and T2) in weeks 19 and 20.

Study burden and risks

Time investment:
- 4 visits to the hospital for the first and seconds assessments (body composition, DEXA scan, strength test, endurance test, venous blood sampling, muscle biopsy, questionnaires) before and after chemotherapy: each visit will last 3 hours
- questionnaires will be repeated after 9 weeks of chemotherapy: 30-60 min of patients' time

Participation in this study will provide the patients with detailed information about their body composition, and endurance- and strength capacity. We will provide this information at the end of the study, since individual outcomes may influence patients* behaviour regarding diet and exercise during the study. Participation in this study has no major health risks. The endurance- and strength testing may evoke some muscle discomfort. The venous blood sampling and the muscle biopsy can result in a local haematoma, which will resolve within a week.

Contacts

Public
Maxima Medisch Centrum

De Run 4600
5504 DB Veldhoven
NL
Scientific
Maxima Medisch Centrum

De Run 4600
5504 DB Veldhoven
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Female breast cancer patients
- Age between 30-65 years
- 18-weeks of chemotherapy-treatment with Taxotere/Adriamycin/Cyclophosphamide (TAC)

Exclusion criteria

- Participation in an exercise rehabilitation program during the study
- Chronic diseases that influence skeletal muscle tissue characteristics, like type 2 diabetes mellitus, chronic obstructive pulmonary disease, chronic heart failure
- Chronic inflammatory disorders, like rheumatoid arthritis, colitis ulcerosa or Crohn*s disease.
- Musculoskeletal disorders that cause an inability to perform the maximal cycling and strength assessment.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	13
Type:	Anticipated

Ethics review

Approved WMO Date:	24-05-2012
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 25768
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL40186.015.12
OMON	NL-OMON25768