Brown adipose tissue activity and energy metabolism in cachexia induced by cancer or chronic disease

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To study BAT activity and energy metabolism in patients with cachexia induced by cancer or chronic disease.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolism disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON43922

Source
ToetsingOnline

Brief title
Brown adipose tissue activity and energy metabolism in cachexia

Condition

- Metabolism disorders NEC
- Gastrointestinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
'wasting syndrome' 'loss of lean body mass'

Research involving
Human

Sponsors and support

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

Intervention

Keyword: brown adipose tissue, cachexia, cancer, energy metabolism

Outcome measures

Primary outcome

The main endpoint of this study is BAT volume and intensity of activity in SUV in the presence of cancer cachexia, COPD cachexia, and compared to non-cachectic COPD patients and healthy individuals, as assessed by 18F-FDG PET-MRI scanning.

Secondary outcome

Secondary endpoints are the relation of BAT activity to a) total energy metabolism and resting metabolic rate and b) metabolic gene expression in WAT and c) systemic inflammatory and hormonal status. Furthermore the PET-MRI allows detailed body composition phenotyping of cachexia to compare with commonly applied clinical measures (D2O and DEXA). Furthermore, dyspnea or meal-related oxygen desaturation, 6 minute walking test and heart rithm will be evaluated.

Study description

Background summary

Evidence by rodent studies in tumour models with cachexia have shown an association between weight loss and thermogenic activation of brown adipose tissue (BAT), providing evidence for a role of BAT activation in the progression of (cancer) cachexia. . BAT has not been investigated in relation to COPD but a recent rodent model of COPD associated cachexia showed elevated white adipose tissue (WAT) metabolic gene expression and browning of WAT. Previous autopsy samples have shown that high prevalence of BAT in cancer-induced cachexia could be related to the hypermetabolic state of these

patients. Recent introduction of 18F-FDG PET-CT led to more awareness of BAT activity. The observation of BAT in oncology patient staging by 18F-FDG PET-CT scanning as well as the strong correlation between BAT activity and body mass index (BMI) has strengthened the notion that BAT activation may contribute to elevated energy requirements in patients with cachexia. We hypothesize that BAT volume and activity is increased in cachectic patients induced by either cancer or COPD, and contributes to elevated energy metabolic rate. Furthermore, in COPD it is hypothesized that energy expenditure is elevated due to impaired lung mechanics. The recently introduced lung volume reduction procedure by endobronchial valves ia an unique model to test the influence of lung mechanics on energy balance in COPD.

Study objective

To study BAT activity and energy metabolism in patients with cachexia induced by cancer or chronic disease.

Study design

Cross-sectional study: Determine BAT activity in cachectic patients with pancreatic or non-small cell lung cancer, and in cachectic COPD patients, and compare results with healthy individuals and non-cachectic COPD patients, matched for gender, age and BMI in a prospective cross-sectional design.

Intervention

BAT activity: 18F-FDG -PET-MRI-imaging.
Body composition: DXA scanning, D2O and MRI.
Inflammatory and metabolic profile of adipose tissue: abdominal subcutaneous adipose tissue biopsy.
Systemic inflammatory profile: blood sampling
Resting metabolic rate: indirect calorimetry.
Physical activity level: accelerometry.
Total daily energy expenditure: double-labeled water.

Study burden and risks

The total absorbed radiation dose from one 18F-FDG PET-scan after administration of 150 MBq of 18F-FDG is 2.9 mSv, which is considered as a low risk. The other measurements and procedures have very low risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Cachectic pancreatic cancer patients:
* Stage I-IV pancreatic cancer patients;
* The diagnostic criterion for cachexia is unintentional weight loss more than 5% over the past 6 months or more than 2% in individuals with a body-mass index < 20 kg/m2 and muscle wasting assessed by DXA;
* Age * 30 years;
* Gender: male and female;

Cachectic NSCLC patients:
* Stage I-IV NSCLC patients;
* The diagnostic criterion for cachexia is unintentional weight loss more than 5% over the past 6 months or more than 2% in individuals with a body-mass index < 20 kg/m2 and muscle wasting assessed by DXA;
* Age * 30 years;
* Gender: male and female;;Cachectic COPD patients:
* COPD GOLD I-IV (COPD patients with and without receiving lung volume reduction by

endobronchial valves);
* The diagnostic criterion for cachexia is unintentional weight loss more than 5% over the past 6 months or more than 2% in individuals with a body-mass index < 20 kg/m2 and muscle wasting assessed by DXA;
* Age * 30 years;
* Gender: male and female;;Non-cachectic COPD patients:
* COPD GOLD I-IV (COPD patients with and without receiving lung volume reduction by endobronchial valves);
* Age * 30 years;
* Gender: male and female;;Healthy individuals:
* Age * 30 years;
* Gender: male and female;;Emphysematous COPD patients:
* Receiving lung volume reduction by endobronchial valves
* Age * 30 years;
* Gender: male and female;

Exclusion criteria

Cachectic pancreatic cancer patients:
* Uncontrolled Diabetes Mellitus;
* Patients with severe clotting disorder;
* Patients with an active second malignancy;
* Psychological unstable persons presumed unfit to perform the measurements, including claustrophobia;
* Persons unable to lie or sit still for 1-2 hours;
* Oxygen therapy;
* Pregnant subjects;
* Subjects unable to undergo MRI (e.g. pacemaker; neurostimulator; ICD or leads; Foley bladder catheter; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; vascular clips; denture, which contains magnets);
* Subjects that received high doses of radiotherapeutic radiation of the neck and/or upper chest in their medical history;
* Persons that received cervical or thoracic sympathectomy or have a nerve dysfunction which is likely to influence sympathetic nerves;
* The use of medication that influences the sympathetic nerve system: ß-blockers, *-blockers, central anti-hypertensives, certain anti-depression drugs (MAO inhibitors, tricyclic anti-depressives), reserpine, cocaïne, calciumblockers, labetalol, and certain tranquillizers (fenothiazines).;Cachectic NSCLC patients:
* Uncontrolled Diabetes Mellitus;
* Patients with severe clotting disorder;
* Patients with an active second malignancy;
* Psychological unstable persons presumed unfit to perform the measurements, including claustrophobia;
* Persons unable to lie or sit still for 1-2 hours;

* Oxygen therapy;
* Pregnant subjects;
* Subjects unable to undergo MRI (e.g. pacemaker; neurostimulator; ICD or leads; Foley bladder catheter; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; vascular clips; denture, which contains magnets);
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* Uncontrolled Diabetes Mellitus;
* Patients with severe clotting disorder;
* Patients with an active second malignancy;
* Psychological unstable persons presumed unfit to perform the measurements, including claustrophobia;
* Persons unable to lie or sit still for 1-2 hours;
* Oxygen therapy;
* Pregnant subjects;
* Subjects unable to undergo MRI (e.g. pacemaker; neurostimulator; ICD or leads; Foley bladder catheter; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; vascular clips; denture, which contains magnets);
* Subjects that received high doses of radiotherapeutic radiation of the neck and/or upper chest in their medical history;
* Persons that received cervical or thoracic sympathectomy or have a nerve dysfunction which is likely to influence sympathetic nerves;
* The use of medication that influences the sympathetic nerve system: ß-blockers, *-blockers, central anti-hypertensives, certain anti-depression drugs (MAO inhibitors, tricyclic anti-depressives), reserpine, cocaïne, calciumblockers, labetalol, and certain tranquillizers (fenothiazines).;Non-cachectic COPD patients:
* Uncontrolled Diabetes Mellitus;
* Patients with severe clotting disorder;
* Patients with an active second malignancy;
* Psychological unstable persons presumed unfit to perform the measurements, including claustrophobia;
* Persons unable to lie or sit still for 1-2 hours;
* Oxygen therapy;
* Pregnant subjects;
* Subjects unable to undergo MRI (e.g. pacemaker; neurostimulator; ICD or leads; Foley bladder catheter; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; vascular clips; denture, which contains magnets);
* Subjects that received high doses of radiotherapeutic radiation of the neck and/or upper

chest in their medical history;
* Persons that received cervical or thoracic sympathectomy or have a nerve dysfunction which is likely to influence sympathetic nerves;
* The use of medication that influences the sympathetic nerve system: ß-blockers, *-blockers, central anti-hypertensives, certain anti-depression drugs (MAO inhibitors, tricyclic anti-depressives), reserpine, cocaïne, calciumblockers, labetalol, and certain tranquillizers (fenothiazines).;Healthy individuals:
* Psychological unstable persons presumed unfit to perform the measurements, including claustrophobia;
* Persons unable to lie or sit still for 1-2 hours;
* Pregnant subjects;
* Subjects unable to undergo MRI (e.g. pacemaker; neurostimulator; ICD or leads; Foley bladder catheter; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; vascular clips; denture, which contains magnets);
* Subjects that received high doses of radiotherapeutic radiation of the neck and/or upper chest in their medical history;
* Persons that received cervical or thoracic sympathectomy or have a nerve dysfunction which is likely to influence sympathetic nerves;
* The use of medication that influences the sympathetic nerve system: ß-blockers, *-blockers, central anti-hypertensives, certain anti-depression drugs (MAO inhibitors, tricyclic anti-depressives), reserpine, cocaïne, calciumblockers, labetalol, and certain tranquillizers (fenothiazines).;Emphysematous COPD patients:
* Patients with an active malignancy;

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-07-2015

Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	19-03-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-08-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-02-2017
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
ClinicalTrials.gov	NCT02500004

Register	ID
CCMO	NL51402.068.14