Adipose tissue depot-specific differences in adipocyte function and inflammatory mediators in patients with type 2 diabetes mellitus and cardiovascular disease

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Primary Objective: In this study we investigate the adipose tissue depot-specific differences in adipocyte function and inflammation in patients with T2DM and subjects suffering from CVD compared to healthy subjects.Secondary Objective: Characterize...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON33838

Source
ToetsingOnline

Brief title
Adipose tissue characteristics in patients with T2DM and in CVD

Condition

- Diabetic complications
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Adipose tissue chronic low-graded inflammation, inflammation of the adipose tissue

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Subcutaneous adipose tissue (SAT), Type 2 Diabetes mellitus (T2DM), Vascular disease, Visceral adipose tissue (VAT)

Outcome measures

Primary outcome

To determine adipocyte (dys)function in both visceral and subcutaneous adipose tissues in the three different study groups: adipocyte differentiation capacity, insulin sensitivity, and cell surface in the two different adipose tissue depots.

To determine the state of inflammation in both visceral and subcutaneous adipose tissues in the three different study groups: measure adipose tissue macrophage and lymphocyte infiltration, characterize the macrophage subsets in the visceral and subcutaneous adipose tissue.

Secondary outcome

Anthropometric measurements: BMI and WHR; the circumference of the waist as a measure of degree of abdominal obesity.

Plasma levels of: insulin, glucose, free fatty acids, lipids (total triglyceride and total cholesterol with the VLDL, LDL and HDL sub fractions), adipokines (adiponectin, leptin etc.) and cytokines (IL-1, IL-6, IL-8, MCP-1, TNF-α etc.).

Activation state of thrombocytes as a surrogate marker for cardiovascular risk.

Study description

Background summary

Type II diabetes mellitus (T2DM) is one of the most common disorder today and has reached epidemic proportions in many countries. T2DM is characterized by defects in insulin secretion, failure to suppress hepatic glucose output, and impaired glucose uptake in peripheral tissue as skeletal muscle and adipose tissue. Besides insulin resistance, other factors such as hyperglycaemia and inflammation play a central role in the pathogenesis of this disease. Eventually, this leads to an 2-4 fold increase in cardiovascular morbidity and mortality. A significant contributor to the rising prevalence of T2DM and cardiovascular disease risk in many developed nations is an increase in body fat. The prevalence of obesity is grown rapidly worldwide and reaching epidemic proportions in developed countries.
Adipose tissue is a highly metabolic active tissue affecting a lot of tissues like the liver, skeletal muscle and vasculature. Adipose tissue originates from visceral and subcutaneous depots, with different metabolic characteristics. Accumulation of the adipose tissue mass is associated with a disturbed fat distribution, abnormal secretory functions of enlarged adipocytes, and increased infiltration of macrophages and lymfocytes into the adipose tissue, leading to impaired lipid and glucose homeostasis, and inflammation. Therefore, the adipose tissue associated with a more pro-inflammatory state might play a central role in the link between obesity, insulin resistance and cardiovascular disease.

Study objective

Primary Objective: In this study we investigate the adipose tissue depot-specific differences in adipocyte function and inflammation in patients with T2DM and subjects suffering from CVD compared to healthy subjects.

Secondary Objective: Characterize and quantify different cell populations residing in the two adipose tissue depots from subjects with T2DM, subjects suffering vascular disease and healthy controls.

Study design

In this observational study, the functional and morphological differences in both visceral and subcutaneous adipose tissue will be compared in subjects suffering from T2DM, vascular disease and healthy controls without insulin resistance and vascular disease.
Therefore, paired samples of visceral adipose tissue and subcutaneous adipose tissue will be obtained from forty five male or female patients (were the ratio men to women in the three study groups will be similar) recruited at the

department of vascular and abdominal surgery. The surgical procedures includes: cholecystectomy, abdominal hysterectomy and other routine procedures. During surgery, adipose tissue biopsies of approximately five grams will be obtained from both the abdominal subcutaneous and omental visceral depots.

Study burden and risks

The extra burden for the subjects associated with this study is that blood will be drawn, without an extra injection (on top of the blood that will automatically be drawn for the routine surgical procedure). Further, there is a small change that bleeding might occur at the place were the adipose tissue biopsies will be obtained, but this could be healed by the present surgeons. This study is not directly beneficial for the individual subjects, but the results obtained from this study might increase the understanding of the role of the different fat depots in relation to the development of CVD.

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

Control subjects (males and females): Age: 40-60 yrs, BMI: 25-30 kg/m2, plasma glucose < 6.1mM ;Type 2 diabetes mellitus (T2DM) patients (males and females): subjects diagnosed with the disease T2DM, age: 40-60 yrs, BMI: 25-30 kg/m2;Subjects suffering cardiovascular disease (males and females): subjects diagnosed with peripheral vascular disease, history of myocardial infarction, angina pectoris, age: 40-60 yrs, BMI: 25-30 kg/m2

Exclusion criteria

Control group: presence of a chronic or acute inflammation and/or autoimmune disorder, insulin resistance;Type 2 diabetes mellitus (T2DM) patients: presence of a chronic or acute inflammation and/or another autoimmune disorder ;Subjects suffering cardiovascular disease: presence of another chronic or acute inflammation and/or autoimmune disorder, insulin resistance

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:	Recruiting
Start date (anticipated):	05-01-2010
Enrollment:	45
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	07-08-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL24406.091.09