The role of perivascular adipose tissue in the regulation of insulin sensitivity through muscle microvascular recruitment in non-obese and obese individuals

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Ethical review	Approved WMO
Status	Pending
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON42523

Source
ToetsingOnline

Brief title
PVAT, metabolism and vascular health

Condition

- Heart failures
- Diabetic complications
- Vascular disorders NEC

Synonym
Diabetes

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: VIDI grant

Intervention

Keyword: BMI, Capillary recruitment, insulin sensitivity, PVAT

Outcome measures

Primary outcome

Functional and inflammatory properties of PVAT will be quantified and correlations with whole-body and microvascular insulin sensitivity will be analysed. Vasoreactivity of skeletal muscle arterioles with and without perivascular adipose tissue will be studied. We will measure markers of low-grade systemic inflammation and adipocytokines (IL-6, IL-8, leptin, TNF-*, MCP-1, adiponectin, resistin and PAI-1, fibrinogen) .

Pearson's and Spearman correlation analyses will be conducted as appropriate to select the variable that is best correlating with insulin sensitivity.

step-wise multivariate linear regressions will be performed to examine the relations between two variables, controlling for anthropometry and systemic inflammation, and standardized betas (B) are reported.

Secondary outcome

Pearson's and Spearman correlation analyses will be conducted as appropriate.

Correlations of microvascular recruitment in the heart will be correlated in a regression analysis using PVAT properties, anthropometric properties and inflammatory properties.

Study description

Background summary

Despite the central role of obesity in the pathogenesis of diabetes mellitus type 2 (DM2) and cardiovascular diseases (CVD), a large subgroup of obese individuals is metabolically healthy. Perivascular adipose tissue (PVAT) probably plays a role in the regulation of local muscle perfusion and glucose uptake. To what extent PVAT determines the metabolic phenotype of obese individuals is still largely unknown.

Study objective

We aim to study the role of PVAT in regulation of vascular function, tissue perfusion and glucose uptake in muscle. We hypothesize that PVAT determines insulin-induced vasoreactivity when studied ex vivo and correlates with insulin-induced microvascular recruitment in skeletal muscle and metabolic insulin sensitivity independent of anthropometry and systemic inflammation. As a secondary objective we want to test if insulin-induced microvascular recruitment in the myocardium correlates with PVAT properties, anthropometry and systemic inflammation .

Study design

This is an observational study in healthy male subjects exhibiting a wide range of BMI's. We will study metabolic insulin sensitivity combined with the assessment of vascular insulin sensitivity in vivo, We will also measure systemic levels of inflammation and other anthropometric parameters to include in our analyses. At the final visit to the clinic, we will obtain a skeletal muscle biopsy to study ex vivo the effects of insulin on microvessels isolated from the biopsies in a pressure myograph with and without their surrounding PVAT, and study the characteristics of PVAT using different in-vitro and ex-vivo assays.

Study burden and risks

Subjects will visit the clinical research unit three times. On the first visit, they will undergo basic physical examination and blood samples will be collected. On the second visit, subjects will undergo a Hyperinsulinemic-euglycemic clamp (HEC), with microvascular measurements (CEU for the skeletal muscle and the heart). The third visit is to do the muscle biopsies. Risks associated with these measurements consist of (not necessarily) myalgia and bleeding after biopsy, risks of hypoglycaemia or hyperglycaemia during HEC, headache, nausea, transient pulmonary hypertension and allergic reactions during CEU (rare). Bruising and local pain in the antecubital fold

may be experienced during and after placement of venous catheters and/or during blood sampling. As a compensation for their time and effort, as well as the burden of the invasive procedures, subjects will receive ¤200 after completion of the investigation. Burden and risk of participation are limited.

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

- Male
- Caucasian
- age 18-60 years
- BMI is *23 and <40 kg/m2
To obtain enough variation between individuals 30 individuals with a wide range of BMI will be recruited:

o 10 individuals with a BMI 23-28
o 10 individuals with a BMI 28-34
o 10 individuals with a BMI 34-40

Exclusion criteria

- Documented CVD
- Diabetes mellitus
- Stage 2 hypertension (resting blood pressure >160/100 mmHg)
- History of severe inflammatory conditions in the past 15 years
- Recent infections
- recent history (<12 months) of high alcohol use > 4 U/day, more than 3 days in a row
- Use of medication potentially affection insulin sensitivity, microvascular function or inflammation
- Use of anticoagulants (types Warfarin and Coumadin derivatives) that can increase the risk of bleeding during the muscle biopsy (exception is made for aspirin).
- Malignancies (except those of the skin), renal and hepatic diseases.
- Smoking
- Recent (<6 months) marked (>10%) changes in body weight.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2016
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	22-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL54182.029.15