The role of perivascular adipose tissue in the regulation of insulin sensitivity through muscle microvascular recruitment in individuals with obesity or type 2 diabetes before and after bariatric surgery.

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

Summary

ID

NL-OMON43075

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

From the pre- and post operative time points we will study functional and inflammatory properties of PVAT and correlate them with whole-body and microvascular insulin sensitivity. We will correct for anthropometry and systemic inflammation and circulating adipocytokines (IL-6, IL-8, leptin, TNF-*, MCP-1, adiponectin, resistin and PAI-1, fibrinogen) .

Secondary outcome

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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. To further elucidate the role of PVAT in human (patho)physiology, we want to study the phenotypical changes that PVAT undergoes after weight loss and how these changes influences vascular and whole body insulin sensitivity. For these endpoints, patients undergoing gastric

bypass bariatric surgery are to be included in this study.

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.We aim to further study the effects of weight loss on the properties of PVAT. As a secondary objective we want to test if insulin-induced microvascular recruitment in the myocardium correlates with PVAT properties, anthropometry and systemic inflammation. We also want to measure intimal-media thickness of the radial artery and the amount of PVAT of the radial artery and whether they change before and after the surgery.

Study design

This is an observational study in relatively healthy (no DM2, no hypertension, no hyperlipidemia, or other CVDs) and type 2 diabetic obese females (BMI >35), who will undergo bariatric surgery through standard care. At two time points corresponding to before and after (12 weeks) the surgery, we will study the following variables: metabolic insulin sensitivity and vascular insulin sensitivity in vivo. We will also measure systemic levels of inflammation and other anthropometric parameters to include in our analyses. Corresponding to the same two pre- and post operative time points, we will obtain skeletal muscle and subcutaneous adipose tissue biopsies to study the characteristics of PVAT using different in-vitro and ex-vivo assays. participants will wear the accelerometer device for one week time before the operation and another one week 12 weeks after their operation to measure the amount of movement the participants make.

Study burden and risks

Participants will visit the clinical research unit twice times. On the first visit (6 hours duration), subjects will undergo a Hyperinsulinemic-euglycemic clamp (HEC), with microvascular measurements (CEU for the skeletal muscle and the heart). Thereafter, participants will undergo another skeletal muscle biopsy under local anesthesia.The participants will wear an accelerometer during 7 consecutive days after the testing day.

During their scheduled bariatric surgery, the surgeon will obtain the visceral adipose tissue biopsies.

On the second visit (12 weeks after their operation), subjects will undergo a similar test day to their first visit (HEC and CEUS, intima-media thickness

measurement and another skeletal muscle biopsy from the other leg). The participants will wear an accelerometer during 7 consecutive.

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 ¤340 after completion of the investigation. Burden and risk of participation are limited.

Control subjects will visit the CRU twice: pre-operative and 12 weeks post-operative CEUS and HEC measurements. They will not receive skeletal muscle biopsies. Control subjects will receive 200 euros as a compensation for their time and effort.

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

Female -Caucasian -age 18-55 years -BMI is *35 kg/m2
Bariatric surgery participants getting an operation at the OLVG, location West. Control participants getting a cholecystectomy at the OLVG west.

Exclusion criteria

Documented CVD -Stage 2 hypertension (resting blood pressure >160/100 mmHg) -Obstructive sleeping apnea syndrome (OSAS). -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):	02-01-2017
Enrollment:	36

Type:	Anticipated

Ethics review

Approved WMO Date:	16-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-01-2017
Application type:	Amendment
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	NL57982.029.16