Atherosclerosis and the Innate immune system in patients with Diabetes

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To characterize phenotypical parameters, cytokine production and epigenetic characteristics of monocytes in patients with diabetes mellitus type 2, stratified according to antidiabetic treatment regime. Ex vivo exploration of the conditions which...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON44284

Source
ToetsingOnline

Brief title
AID

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arterial wall thickening, atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Horizon 2020 beurs

Intervention

Keyword: Atherosclerosis, Cardiovascular disease, Diabetes, Immune system

Outcome measures

Primary outcome

We will compare monocyte expression of pro-atherogenic markers, cytokine production, epigenetic changes and trans-endothelial migration between diabetes patients and controls, and asses differences between patient groups.

Furthermore, changes in these parameters after ex vivo incubation with stimuli and current and novel anti-inflammatory therapies will be assessed.

Secondary outcome

N.A.

Study description

Background summary

Patients with diabetes mellitus have an over tenfold lifetime risk for cardiovascular (CV) disease. Chronic inflammation plays a key role in the pathogenesis of atherosclerotic CV disease and transduces many of the CV risk factors. Previous studies have appropriated a central role for monocytes, which may exhibit prolonged pro-inflammatory phenotypes due to epigenetic reprogramming mediated by hyperlipidemia. Similar epigenetically mediated pro-inflammatory effects are thought to occur in patients with diabetes, providing specific targets for novel anti-inflammatory therapies. However, research addressing these changes in this heterogeneous group is lacking.

Study objective

To characterize phenotypical parameters, cytokine production and epigenetic characteristics of monocytes in patients with diabetes mellitus type 2, stratified according to antidiabetic treatment regime. Ex vivo exploration of the conditions which lead to the pro-inflammatory activation of monocytes and examination of its reversibility by current and novel anti-inflammatory

treatment options.

Study design

This study is designed as a single centre observational study. After screening for eligibility, all subjects will undergo cardiovascular risk assessment and laboratory testing. Monocyte phenotype (flow cytometry, gene expression and protein expression) as well as functionality (cytokine production, trans-endothelial migration) and epigenetic changes (methylation / acetylation markers) will be analysed. The effect of ex vivo anti-inflammatory treatment on these parameters will be assessed.

Study burden and risks

The burden and risks of participating in this study are estimated to be low. The amount of visits will be limited to a maximum of two, in which patients will undergo standard cardiovascular risk assessment once, with a maximal blood withdrawal of 82 ml per visit.

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

Patients
- Aged 18 years or older
- Diagnosed with diabetes mellitus type 2 ;Control subjects
- Age 18 years or older
- No history of diabetes mellitus or impaired glucose tolerance
- No history of cardiovascular events
- No medication use

Exclusion criteria

Exclusion criteria for all subjects
- Known malignant disorders or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator.
- Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study.
- History of cardiovascular event within the last 3 months.
- Clinical signs of acute infection and/or CRP > 10 mg/L.
- The use of chronic immunosuppressant drugs or antibiotics in the last 6 weeks.
- Chronic use of anti-inflammatory drugs.

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):	15-01-2018
Enrollment:	640
Type:	Actual

Ethics review

Approved WMO

Date:	21-12-2017
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	NL63927.018.17