The Innate Immune System in Atherosclerosis

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The main objectives of this study is to see if changes in the innate immune system can be found in diseases associated with increased risk for atherosclerosis

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

Summary

ID

NL-OMON40196

Source
ToetsingOnline

Brief title
ISA

Condition

- Diabetic complications
- Autoimmune disorders
- 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: CVON Genius beurs

Intervention

Keyword: atherosclerosis, innate immunity, monocytes

Outcome measures

Primary outcome

The main study parameters are the trans endothelial migration capability and

subtyping of monocytes in relation to underlying disease (activity).

Secondary outcome

Other important study parameters include epigenetic changes of monocytes and

differences in cytokine production after stimuli.

Study description

Background summary

Atherosclerosis is the main cause of cardiovascular disease. It is a progressive disease, characterized by the formation of plaques in the vessel wall. After a long asymptomatic period, patients with atherosclerosis can present with symptoms of impaired blood flow due to stenosis (e.g. stable angina pectoris, claudicatio intermittens) or with acute complications due to plaque rupture (e.g. myocardial infarction, ischemic stroke). Many diseases affecting the immune system are associated with enhanced atherosclerosis, independent of traditional risk factors. Recent findings indicate the importance of the innate immune system and monocytes in the development and progression of atherosclerosis. Several disease entities with a pro-inflammatory phenotype, such as chronic kidney disease, diabetes, rheumatoid artritis, Crohn*s disease and psoriasis, are marked by an increased association with cardiovascular morbidity and mortality. Interestingly, in some of these diseases, the suggestion has already been made that prolonged activity of monocytes can be found, even when the stimulus is evaded. Moreover, Recent data highlights the ability of LDL cholesterol to cause arterial wall inflammation and monocyte hyperreactivity. Recently, it has been shown that infection with candida albicans can lead to epigenetic changes on monocytes, rendering them with increased cytokine production, even when the infection is long gone.

Study objective

The main objectives of this study is to see if changes in the innate immune system can be found in diseases associated with increased risk for atherosclerosis

Study design

This study is designed as a single center, observational study. After screening for eligibility, all subjects will undergo cardiovascular risk assessment and laboratory testing. Thereafter assement of transendothelial migration and monocyte activation will be assessd, as well as epigenetics and in vitro stimulation assays.

Study burden and risks

The results of this study contribute to the understanding of the involvement of the innate immune system in atherosclerosis, thereby contributing to risk stratification in individual patients and testing of new anti-atherosclerotic treatment. Individual subjects will gain no direct benefit from this study. The risk of participating in this study is estimated to be low. The patients will visit the hospital on 1 occasions for medical history, cardiovascular risk assessment and blood withdrawal with a maximum of 156 ml.

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

Group A: 40 Healty control subjects
- Aged 18 years or older;Group B: 40 Chronic kidney disease (CKD) patients
- Aged 18 years or older
- 20 CKD stages 3 and 4 (GFR: 15-60 ml min-1) and
- 20 Kidney transplant donors with GFR: 15-60 ml min-1 for a duration of at least 3 months
- Non inflamed (CRP <10);Group C: 20 patients with rheumathoid artritis, currently in remission as assessed by disease activity score <2,6
- Aged 18 years or older
- Non inflamed (CRP <10);Group D: 30 patients with peripheral artery disease defined as: EA-index < 0,9 and validated PAD with echo duplex, divided into 3 groups:
- 10 patients without DM2
- 10 patients with DM2 on oral glucose lowering therapy only
- 10 patients with DM2 on oral glucose lowering therapy and insulin
- Aged 18 years or older
- Non inflamed (CRP <10);Group E:
60 patients with a diagnosis of hypercholesterolemia, consisting of 3 subgroups
- 20 subjects currently not on statin therapy
- 20 subjects on stable statin therapy (at least 3 months) with LDL levels on target
- 20 subjects on stable statin therapy (at least 3 months) with LDL levels not on target
- Aged 18 years or older
- Non inflamed (CRP <10)

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.
- Clinical signs of acute infection and/or CRP>10;Exclusion criteria for group B: Chronic Kidney Disease
- Diabetic nephropathy
- History of MI/Stroke;Exclusion criteria for group C: Rheumatoid artitis
- History of MI/Stroke;Exclusion criteria for group D: Peripheral artery disease
- MI/Stroke in the last 12 months;Exclusion criteria for group E: Hypercholesterolemia

- MI/Stroke in the last 12 months

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):	28-01-2014
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	07-01-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2014
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	NL47204.018.13