Assessment of endothelial function, accumulation of advanced glycation end products and atherosclerosis in patients with longstanding Rheumatoid Arthritis

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1. Is EC dysfunction, measured by PWA, present RA patients?2. Is EC dysfunction in RA related to EC activation markers (CRP, thrombomodulin, sVCAM, vWF), AGEs, and the presence of atherosclerosis?3. Is EC dysfunction related to traditional…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON32391

Source
ToetsingOnline

Brief title
Endothelial function en AGE accumulation in longstanding RA

Condition

- Joint disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerosis, cardiovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Eigen researchpot

Intervention

Keyword: Advanced glycation endproducts, Atherosclerosis, Endothelial function, Rheumatoid arthritis

Outcome measures

Primary outcome

Small Artery Elasticity (SAE) en Large Artery Elasticity (LAE) gemeten met PWA.

EC Activation Markers (TM, sVCAM-1, vWF, hsCRP), Advanced Glycation

Endproducts (AGE), Intima Media Thickness (IMT)

Secondary outcome

Blood count, ALAT, ASAT, creatinin, cholesterol, triglycerides,

HDL-cholesterol, LDL-cholesterol, CRP, blood pressure, pulse rate, BMI,

smoking, family history for CVD, RA disease activity and joint destruction

Study description

Background summary

The mortality of patients with Rheumatoid Arthritis (RA) is, compared to the general population increased mainly due to cardiovascular disease. This premature atherosclerosis can not be explained by the presence of the traditional cardiovascular risk factors. Additional, autoimmunity-related non-traditional risk factors, have been suggested to contribute to the development of atherosclerosis in these patients
Activation and dysfunction of endothelial cells (EC) are considered the first steps in the atherosclerotic process.
Indeed, endothelial activation markers like vascular cell adhesion molecule-1 (VCAM-1), thrombomodulin (TM) and von Willebrand factor (vWF) are increased in RA patients. As a result of EC activation and oxidative stress other events occur, like the formation of advanced glycation endproducts (AGEs). AGEs are a

class of compounds resulting from glycation and oxidation of proteins, lipids or nucleic acids. The accumulation of AGEs in the vessel wall has also been related to the development of atherosclerosis
Endothelial function and the role of AGEs in the development of atherosclerosis in RA are still poorly studied. As EC dysfunction informs about the earliest stages of the atherosclerotic process it provides the opportunity to intervene in this stage in order to prevent manifest cardiovascular disease
EC dysfunction can be detected by several techniques. Flow-mediated dilation, measuring the response to reactive hyperemia, is most commonly used. Indeed, impaired endothelium dependent vasodilatation was shown in young RA patients without traditional cardiovascular risk factors or cardiovascular events. However, the method has a poor reproducibility and informs about larger vessels. EC dysfunction can also be detected non-invasively by pulse-wave analysis (PWA), which measures large and small artery elasticity (LAE and SAE, respectively) [24]. Unlike FMD, PWA is more readily available and well-tolerated. Several studies have shown that PWA is a reproducible method to assess EC function in vivo.
AGE accumulation can by measured by autofluorescence with the AutoFluorescence Reader (AFR, patent PCT/NL99/00607) A tool for noninvasive assessment of AGE accumulation in skin.
These two measuremnets will be related to the Intima Media Thickness a surrogate marker for atherosclerosis.

We hypothesise that EC dysfunction, measured by PWA, will be present in longstanding RA patients and that this EC dysfunction is related to EC activation, AGE formation, and the presence of atherosclerosis. To analyse the cause of EC dysfunction, we will investigate all traditional cardiovascular risk factors as well as non-traditional, disease related, factors.
For this cross-sectional study RA patients with disease duration of 10-15 years will be compared with age and sex matched healthy controls,

Study objective

1. Is EC dysfunction, measured by PWA, present RA patients?
2. Is EC dysfunction in RA related to EC activation markers (CRP, thrombomodulin, sVCAM, vWF), AGEs, and the presence of atherosclerosis?
3. Is EC dysfunction related to traditional cardiovascular risk factors or non-traditional, disease related, factors such as cumulative markers of inflammation and/or destruction?

Study design

For this cross sectional study we will approach 50 RA patients with a disease duration of 10-15 years and 50 healthy age and sex matched controls (see power analysis).
All participants will undergo PWA, IMT measurement by ultrasound, and

assessment of AGE accumulation using the AutoFluorescence Reader (AFR). Blood will be taken for analysis and a questionnaire will be administrated. In total this visit will take 1,5 hours.

Study burden and risks

All measurements, the complete visit will take about 1,5 hour. For the RA patients we will try to combine this with a regular visit at the outpatient clinic of the department of Rheumatology.

From RA patients 4 extra tubes of blood (26ml) will be drawn in addition to the 2 regular taken tubes for routine lab. controles at the out-patient clinic.
From the healthy controls a total of 6 tubes (34ml) will be collected for the lab. measurements.
The other measurements (PWA, AGE-accumulation and IMT measurement) are non-invasive.

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

-Rheumatoide arthritis; "American College of Rheumatology criteria for RA"
-disease duration of 10-15 year
-informed consent

Exclusion criteria

Rheumatoid arthritis patients:
-Pregnancy
-Diabetes mellitus (fasting blood glucose * 7.0 mmol/L)
-Renal impairment (serum creatinine *:140 *mol/L)
-Recent Surgery
-Myocardial infarction (MI) or sepsis in the past three months;Healthy age and sex matched controls:
-Pregnancy
-Diabetes mellitus (fasting blood glucose * 7.0 mmol/L)
-Renal impairment (serum creatinine *:140 *mol/L)
-Recent Surgery
-MI or sepsis in the past three 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):	28-08-2008
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL23695.042.08