Endothelial function in Systemic Lupus Erythematosus and Wegener's granulomatosis: associations with traditional and non-traditional cardiovascular risk factors

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We hypothesise that EC dysfunction is present in SLE and WG patients compared to controls. In summary, our hypothesis leads to the following questions:1. Is EC dysfunction, measured by SAE, present in SLE patients?2. Is EC dysfunction related to EC...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON30402

Source
ToetsingOnline

Brief title
Endothelial function in SLE and WG

Condition

- Autoimmune 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: Ministerie van OC&W

Intervention

Keyword: Endothelial cell dysfunction, Pulse-Wave Analysis, Small Artery Elasticity, Systemische lupus erythematosus

Outcome measures

Primary outcome

Small Artery Elasticity (SAE), Large Artery Elasticity (LAE), Intima Media

Thickness (IMT), EC Activation Markers (TM, sVCAM-1, vWF, homocysteine, oxLDL,

hsCRP), Advanced Glycation Endproducts (AGE), Endothelial Progenitor Cells

(EPC)

Secondary outcome

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

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

smoking, family history for CVD

Study description

Background summary

Systemic autoimmune diseases, such as systemic lupus erthematosus and Wegener's granulomatosis, are associated with an increased prevalence of cardiovascular disease. Atherosclerosis is the major underlying cause of CVD, several studies have demonstrated the presence of accelerated atherosclerosis in SLE and WG, using intima-media thickness (IMT) as a surrogate marker for atherosclerosis. The presence of atherosclerosis could not be explained by the presence of traditional cardiovascular risk factors. Therefore, additional, autoimmunity-related non-traditional risk factors, have been suggested to contribute to the development of atherosclerosis.
Endothelial cell (EC) activation and dysfunction 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 SLE and WG patients, even in inactive disease.
As a result of EC activation other events occur, like the formation of advanced glycation endproducts (AGEs). AGEs are a class of compounds resulting from the glycation and oxidation of proteins, lipids or nucleic acids. The accumulation of AGEs in the vessel wall has been related to the development of atherosclerosis.
EC repair is mandatory and endothelial progenitor cells (EPCs) are supposed to play an important functional role in the repair of damaged endothelium. We recently found that numbers of EPCs are decreased in SLE patients. Moreover, EPCs of SLE patients were functionally impaired and we suppose that these aberrations will contribute to, and even might accelerate, endothelial damage and atherosclerosis in SLE.
Endothelial function in SLE and WG is still poorly studied. Detection of EC dysfunction provides the opportunity to intervene in this early stage in order to prevent cardiovascular disease. EC dysfunction can be detected by several techniques. Flow-mediated dilation, measuring the response to reactive hyperemia, is most commonly used. However, this 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). Unlike FMD, PWA is more readily available and well tolerated.
We hypothesise that EC dysfunction, measured by SAE, will be present in our cohorts of SLE and WG patients. This EC dysfunction is related to EC activation, AGE formation, the number and function of EPCs 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 risk factors. Finally, we want to analyse whether PWA is usable for intervention studies.

Study objective

We hypothesise that EC dysfunction is present in SLE and WG patients compared to controls. In summary, our hypothesis leads to the following questions:

1. Is EC dysfunction, measured by SAE, present in SLE patients?
2. Is EC dysfunction related to EC activation markers, AGEs, levels and functional capacity of circulation EPCs, and the presence of atherosclerosis?
3. Is EC dysfunction related to traditional cardiovascular risk factors or non-traditional factors
4. Can PWA be used in intervention studies?

Study design

For this cross sectional study we will include 40 SLE patients, 40 WG patients, 40 healthy age and sex matched controls (serve as negative controls) and 40 patients with essential hypertension (serve as positive control).

To be informed about test variation in all participants (except WG patients) SAE will be detected twice, in one half of the participants immediately after the first measurement, in the other half of the participants one week after the first measurement. In addition, in all participants both arms will be tested.

Study burden and risks

For half of the participant measurements will take about 2 hours and 30 minutes, measurements will take place on two moments. For the other half of the participants and all WG patients measurement will take about two hours.

We will try to combine a patient's visit to the treating physician with our research.

In SLE and WG patients 3 tubes of blood (28 ml) will be drawn for further analysis. In controls and essential hypertension patients 4 tubes of blood (34 ml) will be drawn.

Participants need to fast and have to refrain from tobacco in the 12 hours before Pulse-Wave Analysis.

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

SLE patients:
- fulfil the American College of Rheumatology criteria for SLE
- 20-65 years of age;WG patients:
- fulfil the American College of Rheumatology criteria for WG
- 20-65 years of age;Patients with essential hypertension
- blood pressure of 140/90 mmHg or more
- age and sex matched to SLE patients;Healthy controls:
- age and sex matched to SLE patients

Exclusion criteria

- pregnancy
- diabetes mellitus
- renal impairment
- MI or sepsis in the past three months
- recent surgery
- clinical history of cardiovascular disease
- cardiovascular conditions that can produce altered blood pressure waveforms: arrythmias, valvular heart disease or congestive heart failure;SLE patients:
- Raynaud's phenomenon

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:	Pending
Start date (anticipated):	01-12-2006
Enrollment:	160
Type:	Anticipated

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	NL14919.042.06