Discovering the Dynamics of Endothelial Shear Stress

Published: 14-11-2011
Last updated: 28-04-2024

2.1 Primary ObjectiveTo determine the effect of endothelial dependent and independent vasodilators on endothelial shear stress in humans. 2.2 Secondary ObjectiveTo determine the association between endothelial shear stress and endothelial function...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON35323

Source
ToetsingOnline

Brief title
DISCOVER

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arteriosclerosis, coronary heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: atherosclerosis, Endothelial function, Endothelium, Shear stress

Outcome measures

Primary outcome

The absolute difference between baseline endothelial shear stress before and after an endothelial dependent and independent vasodilator.

Secondary outcome

The association between the absolute flow-mediated vasodilatation (mm) in the brachial artery and endothelial shear stress in N/m2.

Tertiary outcome: The association between the absolute flow-mediated vasodilatation in the brachial artery and endothelial shear stress in N/m2 during an inflammatory respons.

.

Study description

Background summary

The interaction between blood flow and the endothelium has been proposed to play a role in the atherosclerotic disease process. Low ESS promotes increased permeability and enhanced low-density lipoprotein cholesterol uptake into the artery wall.These processes are known to facilitate arterial remodeling. Furthermore, ESS regulates endothelium-derived NO, which plays a central role in the regulation of large-artery stiffness in vivo. Despite these data from in vitro and animal studies, the relationship between ESS and arterial remodeling and arterial stiffness has not been investigated in vivo in humans. The scarcity of data on this topic is predominantly because accurate quantification methods to estimate ESS in vivo are challenging to create. Most existing approaches either use highly complicated methods such as computed fluid dynamics, which are unmanageable in trials investigating larger populations, or use oversimplified methods that assume Poiseuille flow.Similarly, assessment of arterial stiffness as well as arterial structure is technically difficult. We

therefore developed a noninvasive 3.0-T MRI protocol that enables quantification of all these dimensional and functional aspects in a single MRI scanning session. We based our ESS assessment on velocity gradient modelling comparable to methods previously used by Oyre et al.We determined excellent reproducibility and a role for endothelial stress in arterial remodelling and arterial stiffness in humans. Here, we propose to further elucidate determinants of endothelial shear stress and to establish the relation between endothelial function and endothelial shear stress in humans.

Study objective

2.1 Primary Objective
To determine the effect of endothelial dependent and independent vasodilators on endothelial shear stress in humans.

2.2 Secondary Objective
To determine the association between endothelial shear stress and endothelial function in humans.

2.3. Tertiary Objective
To determine the effect of endothelial dependent and independent vasodilators on wall shear stress during a low grade inflammatory response.

Study design

This is a cross-sectional study.

Study burden and risks

Patients receive no direct benefits. They have to visit the AMC 1-2 times for a four hour visit.
Maximal invasive procedures are the blood withdrawahl and the vaccination (for healthy controls only).
Patients can perceive the FMD as strenuous due to the tight cuff around the upper arm.
Patients will get two different vaso-active medications with a short half-life.
Patient will get a MRI examination.
The associated risk for all procedures is minimal.

Contacts

Public

Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Group A:
1) Healthy individuals aged between 18 and 45 years old.
2) Not known with any clinical significant disease
3) Not using any prescription medication
4) Non-smoking
Group B:
1) Patients aged equal to or greater than (*) 45 years.
2) Known with an elevated LDL cholesterol (LDL > 90th percentile) with or without LDLc lowering therapy

Exclusion criteria

Group A and B: ;1) Current active inflammatory diseases.
2) Any clinically significant medical condition that could interfere with the conduct of the study.

3) Known with hypertension (>15 years) , cardiac hypertrophy, cardiac failure (NYHA class I-IV) or any form of ischemic heart disease.
4) Standard contra-indications to MRI.
5) Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study.
6) Contra-indications to salbutamol and / or nitroglycrine;For group A only:
1) Previous clinical significant vaccination reactions

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):	07-03-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

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	NL37494.018.11