Increased thrombogenicity in patients with atherosclerosis of the peripheral arteries of the lower extremities: a case-control study.

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In PAD patients, the coagulation status of patients with a vascular complication, will be compared (based on test results of the Thrombogram*, Thromboelastometry and MiRNA*s) to the coagulation status of PAD patients without a vascular complication…

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

Summary

ID

NL-OMON38884

Source
ToetsingOnline

Brief title
Changes in the coagulation in patients with peripheral arterial disease

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerosis, Hypercoagulability, peripheral arterial disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Atherosclerosis, Claudicatio Intermittens, Hypercoagulability, PAD

Outcome measures

Primary outcome

1. Thrombogram* measurement in full-blood and PPP

2. Flow chamber assay

3. Thromboelastometry with added tPA

4. Measurement of Mi-RNA*s

Secondary outcome

N/A

Study description

Background summary

Intermittent claudication is the most important symptomatic manifestation of peripheral arterial disease (PAD) and is associated with a significant morbidity and mortality. The pathophysiological processes involved in the occurrence of complications in PAD are: thrombosis and atherogenesis. Exposure of blood to the thrombogenic surface of the ruptured atherosclerotic plaque, is not fully explaining the complications.
In the literature evidence can be found for the role of Virchow*s triad in thrombogenesis, and the generation and course of PAD and related complications. Components of Virchow*s triad are: hypercoagulability, hemodynamic changes and endothelial injury/dysfunction.
PAD patients seem to adhere to these three components, and are thought to have a 'prothrombotic' or 'hyper coagulable status'. The Thrombogram* is a relatively new method to evaluate a patient*s coagulable state by measuring thrombin generation in time. It is a modern *over-all* physiological test which is capable to report the function of the haemostatic-thrombotic system. The Maastricht flow-chamber assay is measuring thrombocyte function in a full-blood sample. Blood will be forced to flow along different thrombogenic surfaces at different velocities. Comparing analyses of thrombocyte activation will be

carried out by using a well-plate based cytrometric assay. Thromboelastometry (ROTEM) with added tPA can give better insights in the build-up and break-down of a blood clot. This viscoelastometric method, carried out in full-blood, providing information about interactions between different coagulation factors, inhibitors of coagulation and cellular components, during the coagulation and fibrinolytic phase, is measured during two hours. Because whole blood is used in this assay, it is more comparable to the in vivo situation, except for the effects of the endothelium. Measurement of Micro-RNA*s; which possibly are involved in the pathological process of peripheral atherosclerosis.

Study objective

In PAD patients, the coagulation status of patients with a vascular complication, will be compared (based on test results of the Thrombogram*, Thromboelastometry and MiRNA*s) to the coagulation status of PAD patients without a vascular complication and to a healthy control group. Both groups will be sex and age matched. Possible differences in thrombocyte function can be investigated under flow, by using the flow chamber assay. The final goal is to develop insight in these relationships and see if PAD patients with a vascular complication (within 1 year after diagnosis), have a different (increased) coagulation status. For this reason they are possibly at risk for progression of the atherosclerotic process and occurrence of further vascular events.

Study design

A mono-centre observational hypothesis generating study, executed as a case-control study. 80 persons will be included, of which 40 PAD patients and 40 healthy controls. The PAD patients are divided into two groups: 20 patients with (cases) and 20 patients without (controls) a vascular complication within 1 year after the diagnosis. All PAD patients will be included from the PAD study (Hypercoagulability and Atherosclerosis-based Vascular Complications in Patients with Peripheral Arterial Disease of The Lower Extremities (MEC 07-02-088)). Cases will be patients from the PAD study, who reached one or more of the following end-points within 1 year of follow-up:

- *vascular load* cerebrovascular
o ischemic TIA
o ischemic CVA
- *vascular load* cardiovascular
o the novo unstable angina
o myocardial infarction
o revascularisation
- *vascular load* abdomen
o mesenteric ischemia
o renal arterial stenosis + hypertension

- *vascular load* peripheral
o increased symptoms of ischemia + Δ Ankle-brachial-index (ABI) >= 0.1
o increased symptoms of ischemia + intervention

PAD patients will be included as *case* if they are diagnosed with or operated because of one or more *vascular load* areas mentioned above.
PAD patients will be included as *controls* if they didn*t reach one of the end-points within 1 year of follow-up in the PAD study.
Forty healthy volunteers (age and sex matched) will be included. These persons will be asked to come to the hospitals once and help us with giving possibility to compare the results with healthy people as well.

Study burden and risks

The non-significant burden and risk to the patients, utilizing the least invasive methods (vein puncture only) in the study, and the great social and scientific relevance of it, makes it of a great importance. The results of the following trial could help medical doctors improve their behaviour with regard to this world-wide spreading disease.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

Universiteitssingel 50
Maastricht 6229 ER
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

Universiteitssingel 50
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients who have entered the PAD study, as PAD the novo with an EAI<0,9, and did (cases) or did not (controls) reach an endpoint within 1 year of follow-up.

Exclusion criteria

- Patients with known coagulopathies (coagulation disorders)
- Pregnancy
- Chronic Inflammatory Disorders
- Anti-phospholipid syndrome
- Malignancies
- Systemic anticoagulation (acenocoumarol, fenprocoumon, dabigatran, rivaroxaban)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-11-2013
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	06-05-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL43266.068.13