Target finding for atherothrombosis in a population of patients diagnosed with peripheral obstructive arterial disease.

Published: 14-02-2018
Last updated: 15-05-2024

Primary objective: To compare the biochemical and functional differences in coagulation and inflammation status in PAD patients with (recurrent) atherothrombotic events and those without events within 1 year of inclusion into the study Objective 2:...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Embolism and thrombosis
Study type	Observational invasive

Summary

ID

NL-OMON55822

Source
ToetsingOnline

Brief title
Target finding for atherothrombosis in PAD patients.

Condition

- Embolism and thrombosis

Synonym
Intermittent claudication, Peripheral artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Bayer,Bayer B.V.

Intervention

Keyword: Atherothrombosis (MeSH), Hypercoagulability, Observational study (MeSH), Peripheral Arterial Disease (MeSH)

Outcome measures

Primary outcome

Number and type of atherothrombotic events: CAD, MI, stroke, limb ischemia, and re-vascularisation, all-cause and cardio-vascular mortality (within 1 year of inclusion into the study).

Secondary outcome

The difference between patients that experienced event(s) within 1 year of inclusion into the study and those that did not for 1) coagulation and inflammation profile (levels of D-dimer, Thrombin-Antithrombin, Thrombin generation, FIX-AT complexes, P-selectin, TNF-, Fibrinogen, CRP, V-CAM, I-CAM, CD40, IL1-, IL8, IL10), 2) the difference in platelet reactivity, 3) the difference in adherence rate, and 4) the sensitivity and specificity of a (newly developed) functional assay.

Other study parameters:

Smoking status, age, gender, BMI (height, weight), diabetes, time since diagnosis, extent of disease (mild/moderate, severe PAD), blood pressure, kreatinin and estimated kreatinin clearance, blood glucose, HbA1c, lipid profile (LDL, HDL, cholesterol, triglycerides), concurrent medication.

Study description

Background summary

Atherosclerosis is and will remain a major health care problem for at least the next decade, and will likely cause many atherothrombotic complications, inducing mortality, morbidity and associated increased health care expenses. In order to optimize care, treatment and prevention, more research should be directed at this serious and yet common problem.

Identification of patients at the highest risk of atherothrombotic complications might help to better target treatment and at the same time provide the opportunity to further characterize the underlying processes contributing to this enhanced risk profile. Until now it remains unclear why atherothrombotic complications occur in some patients, and never occur in other patients diagnosed with PAD.

In a previous study on the role of hypercoagulation in the onset and propagation of PAD, we found limited evidence for a hypercoagulable state in patients with PAD as assessed by Thrombin Generation test (TG; ThrombogramTM). The study showed contra intuitive results of reduced peak height and prolonged lag time; both of these findings are usually associated with reduced coagulability rather than increased coagulability. This finding is however in line with publications of inverse relationships for TG in similar patient populations that showed prolonged lag time associated with recurrent events, and low peak height with decreased time to event free survival. The regulated network of pro- and anti-coagulation driven actions of thrombin makes it imaginable that both low and high thrombin concentrations can be relevant in the pathophysiology of arterial vascular disease and atherothrombosis. Low amounts of thrombin would theoretically provide insufficient drive for protein C activation, to protect against clotting and inflammation. Relatively high thrombin concentrations could overcome locally protective effects of activated protein C to drive protease activated receptor (PAR) mediated cell signalling functions. Another important factor that may influence thrombosis risk, and which is not present in TG testing is platelet reactivity. Therefore further research should include platelet rich plasma or whole blood.

Study objective

Primary objective:
To compare the biochemical and functional differences in coagulation and inflammation status in PAD patients with (recurrent) atherothrombotic events and those without events within 1 year of inclusion into the study

Objective 2:
To validate a (newly developed) functional assay by discriminating patients

with (recurrent) events from those without events within 1 year of inclusion into the study*

Objective 3:
To correlate platelet reactivity by VerifyNow testing or VASP-testing in patients with Clopidogrel, with (recurrent) atherothrombotic events within 1 year of inclusion into the study

Objective 4:
To correlate a compliance tool (ARMS) to laboratory assessment of treatment efficacy as well as to (recurrent) atherothrombotic events within 1 year of inclusion into the study.

*For patients who undergo a new atherothrombotic event, or in case of laboratory findings that require further investigation, repeated sampling will be necessary (with a maximum of 3 times) to adjust the assay cascade according to the findings and to get sufficient material for further analysis (e.g. blood cells or immune cells).

Study design

This is a prospective observational cohort study including consecutive adult patients objectively diagnosed with peripheral artery disease. Eligible patients are those with ABI <= 0.9 and Fontaine-classification II or III at the time of diagnosis.

Patients with mild as well as more severe forms of PAD (but without ulcers) will be included. Patients can be newly diagnosed, but may also be patients with established PAD that are currently followed at the vascular surgery outpatient clinic of the MUMC+.

The follow-up duration will be one year.

Study burden and risks

The study can only be performed in PAD patients, as the study of the nature of the underlying pathophysiology of PAD is the central issue of this investigation. There is limited risk associated with participation in the study, patients will be asked to undergo at least one, and in some instances up to three, venapuncture(s). Other procedures are performed in the context of usual patient care. Study visits will be combined with normal follow up visits at the outpatient clinic. Patients will be asked to fill out a compliance questionnaire once. There is no direct benefit of participation in the study. It is not anticipated that participation in the study will cause physical or physiological discomfort.

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

- Patients diagnosed with peripheral artery disease, both new patients and patients currently in follow-up
- Patients currently using Clopidogrel
- Patient provided signed declaration of consent
- Patients are at least 18 years of age and compos mentis.

Exclusion criteria

- Use of therapeutic doses of anticoagulants (Vitamin K antagonists, DOACs or Low molecular weight heparins).
- Pregnancy, oral contraceptives, or hormone replacement therapy.

- Chronic inflammatory disease (e.g. RA, CU, MC).
- Anti-phospholipid syndrome (APS).
- Active malignancy.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2018
Enrollment:	315
Type:	Actual

Ethics review

Approved WMO

Date:	14-02-2018
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

ID: 21578
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL63235.068.17
OMON	NL-OMON21578