A randomized placebo-controlled double-blind trial studying the effect of single antiplatelet therapy (clopidogrel) versus dual antiplatelet therapy (clopidogrel + aspirin) on the occurrence of atherothrombotic events following lower extremity peripheral transluminal angioplasty

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To assess whether and to what extent dual therapy clopidogrel 75 mg/acetylsalicylic acid 80 mg daily is superior to monotherapy clopidogrel 75 mg daily, in reducing the combined endpoint all-cause death and cardiovascular adverse events after one-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON56168

Source
ToetsingOnline

Brief title
CLEAR-PATH study

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
(chronic) peripheral (occlusive) arterial disease, Narrowed/blockage of arteries in the lower extremities

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Antiplatelet drugs, Arteriosclerosis, Endovascular procedure, Peripheral vascular diseases

Outcome measures

Primary outcome

The primary endpoint is all-cause death and the occurrence of cardiovascular adverse events after 1 year: re-intervention due to any restenosis or re-occlusion or due to acute limb ischemia, the occurrence of any amputation, cerebrovascular event, myocardial infarction, or cardiovascular death.

Secondary outcome

The secondary endpoint is the occurrence of all and major bleeding (following the TIMI bleeding classification and BARC criteria), major adverse cardiovascular events (MACE), and major adverse limb events (MALE). CYP2C19 polymorphisms will be determined to examine if non-responsiveness to clopidogrel predicts outcome. The findings will not change clinical practice within the course of the trial.

Study description

Background summary

Long-term antiplatelet therapy is the standard of care in patients with peripheral arterial disease (PAD) because it reduces atherothrombotic events. Despite this supportive treatment, the atherothrombotic events remain high in PAD patients. In both coronary and cerebrovascular disease dual antiplatelet therapy has proven to reduce atherothrombotic events. However, these results cannot be extracted to PAD patients and there is an evidence gap in antiplatelet therapy in PAD patients. The most recent guidelines on PAD show discrepancies in the choice for dual or monotherapy after endovascular therapy. Related to this, different surveys among vascular surgeons show different use in antiplatelet prescription patterns. Current practice is based on the expert opinion of the physician treating the patient that induces the risk of incoherent choices.

Study objective

To assess whether and to what extent dual therapy clopidogrel 75 mg/acetylsalicylic acid 80 mg daily is superior to monotherapy clopidogrel 75 mg daily, in reducing the combined endpoint all-cause death and cardiovascular adverse events after one-year follow-up in PAD patients who underwent endovascular treatment.
Our hypothesis is that dual therapy with clopidogrel/aspirin will lead to a lower occurrence of atherothrombotic events in patients following endovascular treatment as compared to clopidogrel alone, in absence of risk for major bleedings. This would lead to better clinical outcomes, increased quality of life and an enhanced cost-effectiveness of treatment

Study design

Multicenter double-blind placebo-controlled randomized trial

Intervention

The intervention is comparing two groups: clopidogrel monotherapy (75 mg) plus placebo daily versus dual therapy clopidogrel (75 mg)/aspirin (80 mg) daily.

Study burden and risks

This trial compares the two most commonly prescribed antiplatelet regimens in a randomized fashion. However, only clopidogrel monotherapy is on-label. As such, we anticipate that patients do not have a higher bleeding risk when participating in the study than in general practice. A blood sample for CYP2C19

polymorphisms will be obtained during the intervention. This procedure bears only the minimal risks while there is already access to the blood/vene/arteria during the intervention. Patients do not benefit from participation, since the results of the test will not influence the medical treatment plan. At last, patiënts need to fill in questionnaires every 6 months.

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

To be eligible to participate in this study, a subject must meet all of the following criteria:
1. Lesions of the iliac, femoropopliteal, and/or below-the-knee (BTK) arteries;
2. At least one TASC lesion;
3. Rutherford (1-6) classes with an indication for an endovascular intervention;

4. Proficient understanding of the consequences of enrolment by the patient;
5. Written informed consent by the patient;
6. Age >= 45 years.
And:
7. Eligibility of lesions for;
a. Percutaneous transluminal angioplasty (PTA) or recanalization with or without additional stenting based on prevailing guidelines, or;
b. Hybrid procedure with an endarterectomy of the common femoral artery and additional iliac, femoral or tibial PTA, or;
c. A reintervention within 2 months due to a phased treatment.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Acute (limb) ischemia
2. Reported intolerance or hypersensitivity to the study medications
3. Use of anticoagulant therapy (DOACs or coumarin)
4. Use of non-steroidal anti-inflammatory drugs >2 weeks which cannot be discontinued
5. Patients incompetent of understanding the consequences of enrolment in the trial.
5.6. Patients with a reintervention due to restenosis/reocclusion within 2 months
7. Patients with a hybrid procedure other than endarterectomy of the common femoral artery such as femoral bypass
8. Patients with coagulopathy
9. Patients with a peptic ulcer confirmed by an esophagogastroduodenoscopy in their medical history
10. Patients who are pregnant/contemplating pregnancy/nursing.
11. Patients requiring dialysis
12. Patients with liver failure and at least one of the following criteria;
a. elevated INR value, or;
b. portal hypertension, or;
c. thrombocytopenia <50x10^9/L, or;
d. INR, portal tension, or platelet count are unknown.

Study design

Design

Study type: Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-08-2022
Enrollment:	1696
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aspirin
Generic name:	acetylsalicylic acid
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Plavix
Generic name:	Clopidogrel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-05-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-06-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-11-2022

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-09-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	METC NedMec

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
EudraCT	EUCTR2021-006611-29-NL
CCMO	NL80009.041.21