Immune cell activation following ischemic cerebrovascular events: a multimodal exploratory study

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To explore innate immune cell composition, function and proliferation in the circulation, bone marrow, and atherosclerotic plaque in patients scheduled for elective carotid endarterectomy because of recent ischemic stroke or transient ischemic...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON49930

Source
ToetsingOnline

Brief title
Immune Activation after Stroke

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerosis, Cerebrovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: NHLBI (NIH)

Intervention

Keyword: Bone marrow, Immune system, Monocytes, Stroke

Outcome measures

Primary outcome

1. Markers of macrophage proliferation and activation in the explanted carotid plaque.

2. Markers of proliferation of the HSPCs and the composition and phenotype of the HSPCs in the bone marrow aspirate

3. Number and phenotype of circulating myeloid cells.

Secondary outcome

1. 18F-FDG uptake in the culprit carotid artery (ie the carotid artery that corresponds with the neurological symptoms of the TIA or stroke and will be operated) and the other large arteries (including aorta, carotid arteries, iliac arteries)

2. 18F-FDG uptake in the bone marrow

Study description

Background summary

The innate immune system importantly contributes to the pathophysiology of atherosclerotic cardiovascular disease, such as stroke and myocardial infarction. Recurrence rate is particularly high in the first months/year after a first ischemic event. Animal studies have shown that acute myocardial infarction or stroke can activate the innate immune system through effects on bone marrow myeloid progenitors. We hypothesize that this immune system activation drives the high recurrence rate. The current proposal therefore aims to explore the innate immune cell phenotype in patients immediately following an ischemic cerebrovascular event, both in the bone marrow, the circulation, and the atherosclerotic plaque. Knowledge on this mechanism and on how this

mechanism can be non-invasively detected by PET scanning, will contribute to the development of novel pharmacological strategies to reduce cardiovascular disease.

Study objective

To explore innate immune cell composition, function and proliferation in the circulation, bone marrow, and atherosclerotic plaque in patients scheduled for elective carotid endarterectomy because of recent ischemic stroke or transient ischemic attack and relate these findings to FDG-PET imaging of the carotid plaque and bone marrow.

Study design

This study is an exploratory observational study in the Radboud university medical center.

Study burden and risks

As discussed in paragraph 11.4 (in the Research Protocol), the venous blood withdrawal of 40 mls of blood, the bone marrow aspiration, and the FDG-PET do not pose significant health risks for the participants.

We will take various measures to reduce the risk as much as possible.
The radiation dose for the PET-CT scan is in risk category IIb. Our study deliver the required level of benefit (acquisition of knowledge, directly aimed at prevention or cure of disease). There are no known side effects with the use of this radiotracer. As far as the PET aspects of the imaging are concerned, the minimum dose of FDG that provides adequate quantification will be used in all subjects.
All imaging studies will be interpreted by a nuclear medicine phycisian and a report of the findings will be provided which may influence the future care of the subject in line with standard clinical practice. Since some of these participants would not normally have undergone PET, it is possible that their participation in the study could lead to additional clinical workup that would not have occurred without their participation in this study. In some cases, these findings may lead to discovery of additional disease, thus benefiting the participant. If incidental findings unrelated to the study are seen on the research images which should prompt further medical or imaging workup, the subject*s physician will be contacted and recommendations for further workup, will be made. No clinical decisions will be based on the research images

For venipuncture, risks will be minimized by having highly experienced and qualified nurses or physicians performing the procedure (venipuncture) and a highly experienced physician assistant from the department of haematology to perform the bone marrow aspiration.

Given the importance of the data that will be derived from this study, we feel the minimal risk described under 11.4 is proportional.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age >18 years
- Stroke or TIA with signs or ischemia on imaging compatible with the neurological deficit.
- Scheduled for carotid endarterectomy based on current clinical standards

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Severe disability (stay in nursing home).
- Auto-immune or auto-inflammatory disease
- Current use of immunomodulating drugs
- Recent infection with fever >38.5 C < 1 month ago.
- Pregnancy
- Renal insufficiency (MDRD <30 ml/min)
- Allergy for FDG or components thereof
- Breastfeeding

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	10-08-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL78221.091.21