INflammation and cerebral small vessel disease (INSVD) study

Published: 24-05-2022
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To investigate the role of the immune and coagulation system on the progression of cerebral SVD

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON51836

Source
ToetsingOnline

Brief title
INSVD

Condition

- Allergic conditions
- Central nervous system vascular disorders
- Vascular hypertensive disorders

Synonym
immune system, inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: cognition, inflammation, magnetic resonance imaging, small vessel disease

Outcome measures

Primary outcome

White matter ultrastructure as assessed with MRI (being the most sensitive

measure of cerebral small vessel disease) and relate this with markers of the

immune and coagulation system.

Secondary outcome

1. Cognition and clinical (stroke, other cardiovascular disease)

2. BBB leakage on MRI

3.

Study description

Background summary

Cerebral small vessel disease (SVD) describes a set of pathologies affecting the smallest blood vessels in the brain. SVD contributes to up to a fifth of ischemic and hemorrhagic strokes en is the main vascular cause of dementia. On MRI, SVD is marked by different types of lesions, including white matter abnormalities, and small infarcts and hemorrhages. Recent studies indicate that SVD develops slowly over the years, starting presumably decades before the typical MRI lesions become apparent. There is increasing evidence that changes in the immune and coagulation system play a key role in the progression of cerebral SVD, however, it remains unclear exactly how these changes lead to microvascular pathology and the MRI markers of SVD.
In order to increase our insight in the etiology and progression of SVD we want to determine blood and MRI markers of the immune and coagulation system in patients with cerebral SVD and follow them over the course of 2 years.

Study objective

To investigate the role of the immune and coagulation system on the progression

of cerebral SVD

Study design

longitudinal prospective cohort study

Study burden and risks

Patients will be asked to undergo a standardised MRI, blood withdrawal and structured questionaires on medical history and cognition and motor performance. MRI is considered to be safe and without risks, as long all safety measures are adequately followed. To study the integrity of the blood-brain barrier during part of the 3 T MRI scan, patients will receive a gadolinium-based contrast agent. Side effects of injection of this contrast agent occur very incidentally and include mild effects such as nausea, headache and injection site reactions (sense of warm feeling). In case of adverse effects, patients will be treated reasonably and professionally.

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

Patient population
1. Have given written informed consent to participate
2. Be aged 40 years and over
3. Have symptomatic cerebral small vessel disease defined as:
• Clinically symptomatic lacunar infarct in presence of white matter hyperintensities (Fazekas >=1) on MRI
• and/or symptoms of cognitive impairment due to small vessel disease (Fazekas >= 1) with lacunar infarct on MRI
• and/or gait apraxia/motor impairment presumed due to small vessel disease (Fazekas >= 1) with lacunar infarct on MRI
If there is a recent history of stroke, baseline MRI will be scheduled at least 3 months after last stroke to exclude BBB changes secondary to acute infarction.

Healthy control population
1. Have given written informed consent to participate
2. Be aged 40 years and over

Exclusion criteria

Patient population
- unable/unwilling to consent including lack of capacity to consent
- vaccination or infection with fever in preceding month
- any stroke cause other than SVD including:
o Cardioembolic source
o Carotid or vertebral stenosis >50% measured on NASCET criteria
- Myocardial infarction in past year
- Vasculitis
- any chronic disease that could lead to brain lesions mimicking SVD (for example multiple sclerosis)
- contraindications for 3 T MRI
- auto-immune/auto-inflammatory disease
- use of immunomodulating drugs
- Estimated glomerular filtration rate (eGFR) <= 29 ml/min/1.73m2. eGFR needs to have been measured within the past 3 months in case the last measurement was <45ml/min/1.73m2, or within the past 13 months in all other cases.
- Another diagnosed chronic neurological condition (e.g. Alzheimer's,

Parkinson's disease, motor neurone disease, multiple sclerosis).
- Limited life expectancy due to another illness or chronic condition making the 2 year follow-up difficult (e.g. widespread malignancy).

Healthy control population
- Unable/unwilling to consent including lack of capacity to consent
- Contraindications for 3 T MRI
- Vaccination or infection with fever in preceding month
- Any stroke or SVD pathology or symptoms (some white matter hyperintensities are permitted)
- Another diagnosed chronic neurological condition (e.g. Alzheimer's, Parkinson's disease, motor neurone disease, multiple sclerosis)
- Myocardial infarction in past year
- Auto-immune/auto-inflammatory disease
- Use of immunomodulating drugs
- Estimated glomerular filtration rate (eGFR) <= 29 ml/min/1.73m2. eGFR needs to have been measured within the past 3 months in case the last measurement was <45ml/min/1.73m2, or within the past 13 months in all other cases.

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:	Recruiting
Start date (anticipated):	28-12-2022
Enrollment:	100
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	24-05-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-08-2024
Application type:	Amendment
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
ClinicalTrials.gov	NCT05746221
CCMO	NL80258.091.22