MiCRovascular rarefaction in vascUlar Cognitive Impairment and heArt failure - VCI

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Microvascular rarefaction is a major common pathway in the development of VCI and HFpEF; rarefaction and the resultant disorders are driven by comorbidities such as hypertension, aging and diabetes, and the disorders often present together.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON28554

Bron
NTR

Verkorte titel
CRUCIAL-VCI

Aandoening

cerebral small vessel disease, vascular cognitive impairment

Ondersteuning

Primaire sponsor: Maastricht University Medical Center
Overige ondersteuning: EU - HORIZON 2020

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

• Advanced brain MRI markers for microvascular hypoperfusion and dysfunction:
-BBB leakage rate and fractional volume (DCE-MRI)
-grey matter perfusion (ASL-CBF)
-microvascular perfusion volume (IVIM)
-parenchymal diffusivity/microstructural integrity (IVIM)
-macrovascular perfusion (GE-DSC-MRI)
-microvascular perfusion (capillary transit time heterogeneity on GE-DCS-MRI or SE-DSC-MRI)

• Cognitive function: overall and domains of memory, information processing speed, executive function

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Rarefaction, the reduction of microvascular density, is thought to be an important mechanism in the pathophysiology of diseases associated with small vessel disease. Among these diseases are vascular cognitive impairment (VCI) due to cerebral small vessel disease (cSVD) and heart failure with preserved ejection fraction (HFpEF). Both diseases often are present together in a single patient and share identical cardiovascular risk factors such as hypertension, diabetes, obesity and aging. These factors are also involved in rarefaction.
A better understanding of the relevance of microvascular rarefaction, and its underlying mechanisms, is needed to develop markers for diagnosis and therapeutic monitoring of both disorders, and to identify and develop targets for prevention of disease progression.
The program CRUCIAL is an international consortium of European investigators that has launched a major collaborative research program to uncover the pathophysiological role of microvascular rarefaction in small vessel diseases such as VCI and HFpEF. CRUCIAL will determine with advanced imaging techniques in different cohorts of patients the relevance of rarefaction.
CRUCIAL aims 1) to develop novel non-invasive tools to diagnose microvascular health (density and function) in both heart and brain, and 2) to investigate whether microvascular density relates to disease severity.
CRUCIAL-VCI is an observational study that will address these CRUCIAL aims in a population of patients with VCI due to cSVD, and healthy controls.

Objective: The main objective of CRUCIAL-VCI is to determine a surrogate MRI marker for microvascular density in patients with VCI due to cSVD, and to relate this to disease severity expressed as macrostructural brain damage and cognitive function.
The secondary objectives are a) to investigate whether microvascular rarefaction is a specific feature of cSVD and not just an ageing phenomenon, by comparing VCI patients and healthy controls; b) to determine the relationship between cerebral microvascular function and (i) rarefaction in the heart and (ii) microvascular density in the eye and sublingual tissue; c) to identify and characterize mi-RNAs related to rarefaction from circulating endothelial derived microvesicles and the correlation with cerebral microvascular function and structural MRI

markers.

Study design: CRUCIAL-VCI is a single-center observational study.

Study population: 75 patients with VCI due to cSVD and 40 healthy controls. Eligibility is based on meeting the inclusion and exclusion criteria and providing written informed consent before entering the study.

Main study endpoints: VCI and controls: microvascular density as assessed by advanced brain MRI markers for microvascular hypoperfusion and dysfunction; macrostructural brain damage as assessed on brain MRI by validated methods; cognitive function as assessed by a validated standardized cognition test battery. Only in VCI patients, we will also assess cardiac function, vascular density in the eye, sublingual capillary health and RNA in microvesicles.

Doel van het onderzoek

Microvascular rarefaction is a major common pathway in the development of VCI and HFpEF; rarefaction and the resultant disorders are driven by comorbidities such as hypertension, aging and diabetes, and the disorders often present together.

Onderzoeksopzet

NONE

Onderzoeksproduct en/of interventie

none; observational study

Contactpersonen

Publiek

Maastricht UMC+
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0433877058

Wetenschappelijk

Maastricht UMC+
Robert Jan van Oostenbrugge

0433877058

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Inclusion criteria for VCI
VCI due to cSVD defined as:
o visiting a memory clinic or outpatient clinic Neurology;
o cognitive complaints;
o demonstration of a cognitive deficit: MoCA<26 or impairment in at least 1 cognitive domain in neuropsychological assessment
o imaging evidence of cerebral small vessel disease:
 - extensive leukoaraiosis on CT, or
 - (early) confluent WMH on MRI (Fazekas score ≥ 2), or
 - multiple punctate WMH on MRI (Fazekas 1) in combination with lacunar infarcts or microbleeds.
o Age 18 years or older
o Ability to undergo MRI
o Capacity to give written informed consent
o Clinical dementia rating scale ≤1

Inclusion criteria for controls
• visiting the outpatient clinic Neurology with complaints related to the peripheral nervous system (e.g. chronic polyneuropathy, carpal tunnel syndrome or neurogenic claudicatio intermittens).
• No cognitive complaints
• No objective cognitive deficit
• Ability to undergo MRI
• Capacity to give written informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Exclusion criteria for both VCI and controls:
• Inclusion criteria are not met
• Unwillingness or inability to give written consent
• Contraindications to MRI, among which: pacemaker, metallic foreign body, claustrophobia, pregnancy, neurostimulator, other kinds of implanted devices or insulin pump
• Contraindications to gadolinium contrast agent used for MRI, among which allergy or severe renal impairment (eGFR <30 ml/min)
• Other major neurological or psychiatric conditions affecting the brain and interfering with the study design, among which: multiple sclerosis, Parkinson’s disease, alcohol/drug abuse,

major cortical stroke, major neuro-trauma, brain tumors.

Exclusion criteria for cardiac MRI (VCI only)
• Asthma and/or COPD
• Slow heart rhythm (<50 beats per minute)
• Irregular heart rhythm (i.e. atrial fibrillation)
• AV-block II-III
• Sick sinus syndrome
• Prolonged QT-interval
• Hypotension defined as systolic blood pressure less than 90 mmHg
• Decompensatio cordis

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-07-2020
Aantal proefpersonen:	115
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8379
Ander register	METC Maastricht UMC : METC232323

Resultaten