The CAA-HERITAGE study: Hereditary Cerebral Amyloid Angiopathy-Dutch type; Investigating Genealogy and Disease Course

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1. To investigate the size of the HCHWA-D population by identifying all (possible) mutation carriers and their relatives. 2. Study the genealogy and natural disease history of these carriers.3. Get insight in possible genetic, environmental and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON47371

Source
ToetsingOnline

Brief title
The CAA-HERITAGE study

Condition

- Neurological disorders congenital
- Central nervous system vascular disorders
- Vascular haemorrhagic disorders

Synonym
familial amyloid angiopathy, HCHWA-D

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: via de Dutch CAA foundation

Intervention

Keyword: Amyloid Angiopathy, Cerebral, HCHWA-D, Hemorrhage

Outcome measures

Primary outcome

Number of HCHWA-D mutation carriers, their disease expression and other

genetic, environmental and vascular risk factors that could influence their

disease course.

Secondary outcome

not applicable

Study description

Background summary

Cerebral Amyloid Angiopathy (CAA) is the most common cause of lobar, primary intracerebral hemorrhage (ICH) in the elderly. CAA-related vascular damage is caused by accumulation of the Amyloid-β (Aβ) peptide in small and medium-sized vessels in the brain. Aβ is derived from the larger amyloid precursor protein (APP). CAA occurs in a prevalent sporadic form (sCAA) and rare hereditary forms. Hereditary Cerebral Hemorrhage with Amyloidosis Dutch type (HCHWA-D) is a rare, familial variant of CAA caused by a genetic mutation in the APP gene on chromosome 21. There are no available treatment options and the burden of the disease in the affected families is tremendous. Because of its similarities with sCAA, HCHWA-D can serve as a monogenetic model for sCAA and offers the opportunity to study different stages of Aβ accumulation and its relation with clinical symptoms.
Until recently, HCHWA-D has mainly been described in several large families in two coastal villages in the Netherlands. However, mutation carriers that have moved to other parts of the country are being increasingly identified. It is unknown how many mutation carriers there are in the Netherlands. Patients with HCHWA-D suffer from recurrent ICH and dementia starting around the 5th decade

of life, often leading to an early death. The disease course varies between different families and among subjects from the same family. There is only little known about risk factors that contribute to a more aggressive or more benign disease course. The main goal of the study is to set up an extensive database to identify all (possible) mutation carriers and to study the natural history of HCHWA-D. In addition, we aim to get insight in possible other genetic, environmental and vascular rsik factors that may influence the natural disease course. Furthermore, this study proposal will serve as the basis for future follow-up studies (not this proposal).

Study objective

1. To investigate the size of the HCHWA-D population by identifying all (possible) mutation carriers and their relatives.
2. Study the genealogy and natural disease history of these carriers.
3. Get insight in possible genetic, environmental and vascular risk factors that may influence their natural disease course.

Study design

This study is an observational family-based study. The disease course and possible risk factors will be studied retrospectively.

Study burden and risks

Proband and relatives: completion of a questionnaire. Probands will be asked to ask in their families who would like to participate in the study, subsequently provide an address list of relatives who want to participate and to draw a pedigree chart of the family.
Studying HCHWA-D can contribute significantly to the worldwide CAA research, as the Dutch population is the largest and best documented hereditary CAA population. With HCHWA-D we have a monogenic model for CAA which makes it possible to study presymptomatic carriers. Identifying factors that influence the disease course would be valuable to both asymptomatic and symptomatic mutation carriers. Ultimately we hope that a better understanding of HCHWA-D will enable us to define new therapeutic and preventive strategies for sporadic and hereditary CAA.

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

Age >=18 years
Diagnosed with: HCHWA-D with proven mutation; and/or symptoms suggestive of the mutation.
Ability and willingness to provide written informed consent.

Exclusion criteria

Age < 18 years
Inability to give informed consent or obtain informed consent from a legal representative

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-11-2015
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	25-03-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	30-01-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	09-01-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	31-01-2020

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL51777.058.14