The Gaia study

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Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Embolism and thrombosis
Study type	Observational non invasive

Summary

ID

NL-OMON52749

Source
ToetsingOnline

Brief title
The Gaia study

Condition

- Embolism and thrombosis

Synonym
bloodclot in cerebral veins, Cerebral vein thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Eerste geldstroom (geld van Ministerie van OC&W aan universiteiten)

Intervention

- No intervention

Keyword: Cerebral vein thrombosis, Diagnosis, MR Black Blood Imaging, MR Direct Thrombus Imaging

Explanation

N.a.

Outcome measures

Primary outcome

The sensitivity and specificity of MRDTI/BTI for the diagnosis of CVT in
patients with suspected first or recurrent CVT who are referred for MRI/MRV in
the setting of routine clinical practice.

Secondary outcome

1) Achievement of a reproducible MRDTI/BTI scan sequence for CVT;
2) To assess interobserver agreement of the readers of MRDTI/BTI for suspected
CVT.

Study description

Background summary

Cerebral vein thrombosis (CVT), i.e. thrombosis of the intracranial veins and sinuses, is a rare but lethal type of cerebrovascular disease, with 1-month mortality rates of approximately 5.6%, mainly due to cerebral herniation. The clinical presentation of patients with CVT is highly variable and nonspecific, which makes the diagnosis of CVT more difficult than other types of stroke. There is no validated clinical algorithm and there are no specific laboratory tests for the diagnosis of CVT. Fort instance, D-dimer tests cannot safely exclude CVT, due to false negative test results. Thus the diagnosis of CVT mainly relies on neuroimaging tests.
Conventional angiography used to be the gold standard for the diagnosis of CVT, but is rarely used nowadays due to its invasive nature. Computed tomography (CT) is generally the first line imaging test, especially in the acute setting, because of its wide availability. Non-contrast CT, however, is normal in 25-30% of patients with CVT and is therefore mainly used to rule out other conditions such as stroke, tumours or brain abscess.CT combined with CT venography (CTV) enhances the diagnostic accuracy, although its sensitivity is dependent on the thrombus site and is especially poor in the detection of cortical vein thrombosis. Furthermore, CTV requires administration of a iodinated contrast agent with potential renal toxicity or allergic reactions as well as the use of

ionizing radiation. Contrast-enhanced magnetic resonance (MR) combined with venography is commonly considered the 'gold standard' for the diagnosis of CVT. MRI is superior to CT for detecting small cortical venous thrombosis and parenchymal lesions. However, this modality has some limitations with false positive results due to flow artefacts and appearances that can vary depending on the age of thrombosis. Thus, even with the combination of MRI and magnetic resonance venography (MRV), the diagnosis may still be difficult. Because of the better availability of CTV, this has become the diagnostic test of first choice in many, but not all, centers and depending on local preference MRV is often mainly performed in patients with contraindications to CTV, i.e. pregnancy or contrast allergies or for the evaluation of possible other parenchymal lesions. Contrast-enhanced MRV is often only performed in patients with inconclusive CTV and high suspicion for CVT. Importantly, differentiation between old and new thrombosis in patients with a history of CVT is often not possible with current imaging tests. Furthermore, the diagnosis of CVT, especially of cerebral cortical veins, is often delayed because the non-specific symptoms, confirmation of diagnosis relaying on the combination of different imaging tests or requires multiple imaging tests due to non-conclusive results. This delays treatment which potentially may result in death or permanent disability. On the other hand, anticoagulation initiated for a false positive diagnosis may cause major bleeding.

An alternative imaging technique for more accurate diagnosis of CVT is MR Direct Thrombus Imaging (MRDTI)/MR Black Blood Imaging (MRBTI). This technique is in an advanced stage of development (Theia study, NCT02262052) and is close to implementation in clinical practice. The method is based on the formation of methemoglobin in a fresh thrombus leading to shortening of the T1 signal. It does not require contrast administration. Both the diagnostic accuracy (sensitivity 97-100%, specificity 100%) as well as the inter-observer agreement of MRDTI for first and recurrent DVT of the leg were reported to be excellent (kappa 0.89-0.98). Moreover, it was shown to accurately differentiate acute from chronic thrombosis. In previous studies, a high sensitivity (100%) and specificity (95.8-100%) of MRDTI/MRBTI for CVT was reported, as compared to CT, MR and MRV. Importantly, in these two studies the diagnosis of CVT was clearly confirmed or ruled out by the CT, MR and/or MRV and patients with non-diagnostic test results were not evaluated. As stated above, due to variation in venous anatomy, artefacts or difficult to visualize small veins, a final diagnosis often remains unclear even after performing CT(V) and MRI/MRV. In addition to the general advantage of not using ionizing radiation and contrast agents, the added value of MRDTI/BTI for the diagnostic management of CVT lies within this latter patient category. Therefore, we plan to evaluate MRDTI/BTI in patients suspected for first or recurrent CVT and referred for MRI/MVR in the setting of routine clinical practice.

Study objective

The primary objective is to assess diagnostic accuracy of MRDTI/BTI for first

and recurrent CVT in patients referred for MRI/MRV in the setting of routine clinical setting. The secondary objectives are to optimize MRDTI/BTI sequences for imaging CVT and to assess interobserver agreement of MRDTI/BTI for suspected CVT.

Study design

This study is a prospective diagnostic proof of concept study to assess diagnostic accuracy of MRDTI/BTI for patients suspected of (recurrent) CVT and referred for MRI/MRV. Since 1) previous studies has shown that MRDTI/BTI scan may be valuable in the diagnosis of CVT, 2) the sequence can be performed without contrast and 3) the sequence only takes a few minutes of extra scanning time, MRDTI/BTI will be added to the standard MR image procedure in patients with suspected CVT referred for MRV. In the first 5 patients scanned with this updated protocol, an expert laboratory technician will optimize the MRDTI/BTI scan sequences. The final diagnosis and treatment plan is left to the discretion of the treating physician. After the study is completed, the MRDTI/BTI images will be read and adjudicated as *positive* or *negative* by two expert reviewers in an imaging core lab, blinded to other radiological examinations, clinical diagnosis and clinical outcome. The diagnostic standard is the aggregate diagnosis by the same expert reviewers based on all available cerebral imaging (without MRDTI/BTI images), clinical outcome and follow up.

Intervention

nvt

Study burden and risks

This is an observational study; patients do not have direct benefits of participating in this study other than helping in increasing our knowledge of the subject under study. The burden of the study is very limited and includes a telephonic follow up that will take only 5-15 minutes. Patients are not expected to experience harm from study participation.

Contacts

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Trial sites

Trial sites in the Netherlands

HagaZiekenhuis
Target size: 10

Noordwest Ziekenhuisgroep
Target size: 10

Leids Universitair Medisch Centrum
Target size: 43

Haaglanden Medisch Centrum (HMC)
Target size: 10

Radboud Universitair Medisch Centrum
Target size: 10

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients with clinically suspected first or recurrent CVT and referred for MRI/MRV scan in the setting of routine clinical practice
2. Aged 18 years and older
3. Willing and able to give informed consent by patient or legal representative

Exclusion criteria

1. A medical condition, associated illness or co-morbid circumstances that precludes completion of the study procedures (90-day follow-up assessment), including but not limited to life-expectancy less than 3 months

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	29-05-2019
Enrollment:	94
Duration:	3 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	No

IPD sharing statement

Plan to share IPD: Yes

Plan description

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Ethics review

Approved WMO Date:	07-02-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-03-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-01-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Notification accepted Date:	02-06-2025
Application type:	Amendment

Review commission: METC LDD

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
NTR	NL-OMON26664
CCMO	NL66036.058.18
Research portal	NL-008592