Optimizing diagnosis of cerebral vein thrombosis with MRI - The Gaia study

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

Samenvatting

ID

NL-OMON26664

Bron
Nationaal Trial Register

Verkorte titel
The Gaia study

Aandoening

English keywords:
- MRDTI
- cerebral vein thrombosis
- diagnostic

Dutch keywords:
- MRDTI
- cerebrale veneuze trombose
- diagnostiek

Ondersteuning

Primaire sponsor: Leiden University Medical Center (LUMC)
Overige ondersteuning: LUMC

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The sensitivity and specificity of MRDTI for the diagnosis of CVT in patients with suspected first or recurrent CVT and an indication for MRV

Toelichting onderzoek

Achtergrond van het onderzoek

There is an unquestionable need for improved diagnostic approaches for cerebral vein thrombosis (CVT), i.e. thrombosis of the intracranial veins and sinuses. CVT is a rare but lethal type of cerebrovascular disease, with 1-month mortality rates of approximately 5.6%, mainly due to cerebral herniation.[1] 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.[2, 3] There is no validated clinical algorithm and there are no specific laboratory tests for the diagnosis of CVT.[2] Fort instance, D-dimer tests cannot safely exclude CVT, due to false negative test results.[4-6] Thus the diagnosis of CVT mainly relies on neuroimaging tests.[2]

Conventional angiography used to be the gold standard for the diagnosis of CVT, but is rarely used nowadays due to its invasive nature.[2] Computed tomography (CT) is generally the first line imaging test, especially in the acute setting, because of its wide availability.[2, 7] 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.[8] 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 and deep venous CVT.[9-11] Furthermore, CTV requires administration of a iodinated contrast agent with potential renal toxicity or allergic reactions as well as the use of ionizing radiation. Magnetic resonance (MR) combined with venography is the currently diagnostic standard of CVT.[2] MRI is superior to CT for detecting small cortical and deep venous thrombosis and parenchymal lesions.[2, 6, 12, 13] 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.[7] Thus, even with the combination of MRI and magnetic resonance venography (MRV), the diagnosis may still be difficult.[3] 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.[14] This delays treatment which potentially may result in death or permanent disability.[14] 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.[14, 15] 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 [16], 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 with an indication for MR-venography, i.e. being a non-diagnostic CVT and/or contraindication for CTV.

Doel van het onderzoek

The primary hypothesis is that MRDTI/MRBTI will demonstrate acceptable sensitivity and specificity for the diagnosis of CVT in patients with suspected CVT and an indication for MR-venography, i.e. being a non-diagnostic CVT or contraindication for CTV

Onderzoeksopzet

Visit 0 (clinical assessment):

- cerebral computed topography (venography)

Visit 1 (enrolment):

- check for in- and exclusion criteria

- obtain informed consent

- medical history

- clinical examination

- Lab test (d dimer, renal function) (Part of clinical practice, no study proceedings)

- Cerebral magnetic resonance venography and MRDTI/BTI of cerebrum (Part of clinical practice, no study proceedings)

- Treatment decision (Part of clinical practice, no study proceedings)

Visit 2 (90 day follow up)

- recording of death, major bleeding, hospital admission or symptomatic CVT or VTE

Trial schedule:

Year 1: finisch study protocol, permission MEC, MRDTI scans to adjust and optimize the DTI scan sequence in 5 patients, instructing other study sites, including 5-15 patients

Year 2: including 30-50 patients

Year 3: including 15-35 patients, blind evaluation post hoc of MRDTI scans, analyse data, writing article and submit manuscript

Onderzoeksproduct en/of interventie

This study is a prospective, multicenter diagnostic proof of concept study to explore the diagnostic accuracy of MRDTI/BTI in the diagnostic management of suspected CVT and an indication for MRV, which most frequently is a non-diagnostic CTV. 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 based on the results of the MRV, and the MRDTI/BTI images will not be made available to the treating physician and attending radiologist. MRDTI/BTI scans will be assessed post-hoc by two blinded expert readers, and the results correlated to the MRV and clinical outcome of the patients.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Patients with clinically suspected first or recurrent CVT who are referred for MRV scan because of:

o Inconclusive CTV scan, as judged by the (neuro-)radiologist, OR

o Patients with a contraindication for CTV (i.e. contrast allergy, pregnancy)

- Aged 18 years and older

- Willing and able to give informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- A medical condition, associated illness or co-morbid circumstances that precludes completion of the study procedures (MRI and 90-day follow-up assessment), including but not limited to life-expectancy less than 3 months, inability to lie flat, morbid obesity preventing use of MR and claustrophobia;

- Non-diagnostic MRV as judged by the (neuro-)radiologist.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
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:	01-10-2018
Aantal proefpersonen:	87
Type:	Verwachte startdatum

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	NL7005
NTR-old	NTR7195
Ander register	Sec ID following : Protocol Version: 1.2, 2018-05-02

Resultaten

Samenvatting resultaten
none