The value of nerve ultrasound in patients with neurofibromatosis type 1

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON20697

Bron
NTR

Verkorte titel
ZenuwEchografie bij Neurofibromatosis type 1 (ZEN)

Aandoening

Neurofibromotosis type 1

Ondersteuning

Primaire sponsor: Erasmus MC
Overige ondersteuning: None

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- HRUS nerve abnormalities and their characteristics (cross-sectional area, presence or absence of vascularization), measured in 6 nerves and the brachial plexus bilaterally;

- presence or absence neurological deficits. This will be determined with neurological examination (strength of 9 muscle groups bilaterally, sensibility in 5 nerve areas bilaterally, 5 reflexes bilaterally, and questions concerning presence or absence of pain), nerve conduction studies (nerve conduction velocity, distal latency, amplitude of action potential, F-wave latency, H-reflex latency) and on indication electromyography (presence of activity in resting condition, amplitude, duration and number of phases of motor unit potentials, pattern at maximal voluntary activation).

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Individuals with neurofibromatosis type 1 (NF1) are prone to develop benign and malignant tumours of the central and peripheral nervous system. Plexiform neurofibromas arise from multiple nerve fascicles, can grow along the length of a nerve and can also extend into surrounding structures, causing pain and neurological deficits. The relation between morphologic changes of the nerve and pain or neurological deficits is not known. It is not yet possible to predict pain or neurological deficits based upon (early) morphological changes. In areas of an existing plexiform neurofibroma, there is a high risk of developing a malignant peripheral nerve sheath tumour, a tumour with a poor outcome. No quick and cost-effective technique exists so far for examining the peripheral nerves of NF1 patients and screening these patients for peripheral nerve tumours.

Objective: This will be an explorative study to examine the value of high-resolution ultrasound (HRUS) of the peripheral nerves in NF1 patients. The primary objective of this study is to determine HRUS abnormalities in a large group of NF1 patients, and to explore the differences in HRUS abnormalities between patients with or without deficits. A secondary objective is to evaluate the stability and growth of plexiform neurofibromas and the incidence of newly detected nerve abnormalities during two years of follow-up.

Study design: Cross-sectional (observational) study and longitudinal study.

Study population: Adult patients with known neurofibromatosis type 1 who are treated in the outpatient clinic of the Erasmus MC Cancer Institute (Rotterdam).

Intervention (if applicable): Not applicable.

Main study parameters/endpoints: The main study parameters are the number of HRUS abnormalities and their characteristics (cross-sectional area, presence of vascularization) and the presence or absence of neurological deficits.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participation in the study means patients will undergo a standardized neurological examination, nerve conduction studies (NCS) and high-resolution ultrasound (HRUS) twice: as soon as possible after inclusion and two years later. In the case of

neurological deficits, electromyography will also be performed directly after NCS. For patients this will mean two extra visits to the outpatient clinic, in addition to the regular visits to their neurologist. The neurological examination will be performed during regular visits or will be combined with NCS and HRUS. NCS and HRUS will be combined in one extra visit at inclusion and one after two years. If patients want to be informed of the results they will be contacted by phone. Clinical examination and HRUS are painless, NCS and electromyography might cause some physical discomfort. Only electromyography may cause mild adverse events (hematoma, haemorrhage, infection).

Doel van het onderzoek

High-resolution ultrasound (HRUS) is a quick and cost-effective technique to study the morphology of peripheral nerves. Sonographic characteristics of plexiform neurofibromas and MPNST have been described in the literature. Recently, a pilot study with only 16 NF1 patients was conducted by Telleman et al. They found frequent subclinical involvement of the peripheral nerves, including (plexiform) neurofibromas. Nerve conduction studies (NCS) were often normal when ultrasound findings were abnormal, and no clear correlation between the techniques was found. We want to perform an explorative study to examine the value of HRUS in a large group of patients with NF1. We hypothesize that HRUS is a quick and cost-effective technique to examine the peripheral nerves of NF1 patients.

Onderzoeksopzet

The duration of the study will be approximately four years:
- first and second year: recruitment and inclusion of patients, first set of examinations at baseline (see below);
- third and fourth year: reporting the first results of the study, follow-up of the included patients (second set of examinations two years after baseline, see below);
- end of fourth year: reporting the end-results of the study.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Age ≥18 years
- Diagnosed with NF1 (see below for diagnostic criteria)
- Treatment at the outpatient clinic of the Erasmus MC Cancer Institute (Rotterdam)

Criteria for diagnosis NF1:
Two or more of the following clinical features are sufficient to establish a diagnosis of neurofibromatosis type 1:
• Six or more cafe-au-lait macules (>0,5 cm at largest diameter in a prepubertal child or >1,5 cm in post-pubertal individuals)
• Axillary freckling or freckling in inguinal regions
• Two or more neurofibromas of any type or one or more plexiform neurofibromas
• Two or more Lisch nodules (iris hamartomas)
• A distinctive osseous lesion (sphenoid wing dysplasia, long-bone dysplasia)
• An optic pathway glioma
• A first-degree relative with neurofibromatosis type 1 diagnosed by the above criteria

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- comorbidity associated with (poly)neuropathy (e.g. alcoholism, diabetes mellitus)
- comorbidity mimicking neuropathic complaints (e.g. myelopathy)
- inability to give informed consent or to undergo HRUS

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 gestart
(Verwachte) startdatum:	11-07-2019
Aantal proefpersonen:	60
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	12-09-2019
Soort:	Eerste indiening

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	NL8017
Ander register	METC Erasmus MC : MEC-2019-0040

Resultaten