High-resolution ultrasonography of peripheral nerves in neurofibromatosis

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The aim of this study is to further explore ultrasonographic abnormalities of peripheral nerves in patients with NF and their relation with symptoms, findings in neurological examination and electrophysiological characteristics.Primary objective:...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Observational non invasive

Summary

ID

NL-OMON44058

Source
ToetsingOnline

Brief title
HRUS of peripheral nerves in NF

Condition

- Peripheral neuropathies

Synonym
Neurofibromatosis, von Recklinghausen disease

Research involving
Human

Sponsors and support

Primary sponsor: Sint Elisabeth Ziekenhuis
Source(s) of monetary or material Support: Investigator Initiated Onderzoek vanuit de Maatschap Neurologie St Elisabeth - Tweesteden Ziekenhuis

Intervention

Keyword: High-resolution ultrasound, Neurofibromatosis, Peripheral nerves

Outcome measures

Primary outcome

High resolution ultrasonography (HRUS) of the peripheral nerves will be performed according to a HRUS protocol. A 7-18MHz transducer will be used during all examinations. Every nerve will be judged on size, echogenicity and vascularity. Images of the peripheral nerves at anatomical landmarks, or abnormalities will be saved in order to be reviewed at a later stage.

Sonography data and abnormalities will be used as primary outcome measure.

Follow-up 1 year:

Sonography will be performed again after 1 year with use of the same protocol.

primary outcome is the development of sonographic abnormalities over time.

Secondary outcome

Interview

The interview will be focused on symptoms of the patients (e.g. subcutaneous nodules, numbness, pain and loss of strength). The family history specific to neurofibromatosis shall also be asked.

Neurologic examination

The neurologic examination will be performed based on the protocol. Also, there will be attention for atrophy, dysfunction of cranial nerves and deep tendon reflexes.

Electrodiagnostic tests

All patients will be examined according to protocol by electrodiagnostic tests.

Sensory and motor conduction speed will be measured.

The abovementioned data will be collected in order to determine the possible

correlation between those findings and findings in sonography.

Follow-up:

The relationship between development of sonographic abnormalities and

development of clinical symptoms will be used as a secundary outcome.

Study description

Background summary

Neurofibromatosis is a group of genetic diseases which manifests mainly in neurological and cutaneous symptoms. There are three subtypes; type 1 (NF1, Von Recklinghausens disease), type 2 (NF2), and schwannomatosis.

NF1 has the highest incidence (1 in 3 000) and manifests itself by multiple cafe-au-lait spots. Patients have a higher chance to develop peripheral neurofibromas, gliomas of the optical tract and sarcomas. Skeletal deformaties are also seen in NF1. Due to the cafe-au-lait spots and the skeletal deformaties, NF1 is usually diagnosed at a young age [Korf, 2015].

NF2 (incidence 1 in 25 000) manifests itself by bilateral pontine angle tumors, spinal tumors and multiple meningeomas. Patients are often diagnosed in their second decade of life [Evans, 2015].

Schwannomatosis is a rare disease, with an annual incidence of 0.58 per 1 000 000. Patients usually present with multiple symptomatic schwannomas. Patients are often diagnosed around their 4th decade in life [Yohay et al. 2015].

Neurofibromas in NF1 can be located in the skin, but also in peripheral nerves or near a nerve root. They can be plexiform or nodular. These non-cutaneous

neurofibromas can develop in malignant peripheral nerve sheat tumors (MPNST) [Korf, 2015].
Peripheral neuropathies are rarely seen in NF2, since there are mainly abnormalities of the central nervous system [Evans, 2015].
Schwannomas can develop in cranial nerves, nerve roots and in peripheral nerves [Yohay et al. 2015].

Imaging of these abnormalities is in full development. In hte past neurofibromas, schwannomas and MPNSTs were mainly depicted by MRI, since it is highly sensitive in soft-tissue abnormalities. However, MRI is expensive, patients can be claustrofobic and it is impracticle when multiple nerves need to be depicted. Due to the recent development of high-resolution ultrasonography (HRUS) it is possible to depict morphologic abnormalities of peripheral nerves in a cost-effective and patient-friendly way [Goedee 2013].

In recent years, there have been a number of case-reports on HRUS in patients with NF. Irregular, hypoechoic enlargements were seen with hemorrhagic, calcified or necrotic mateerial [Kara 2010, Karabacak 2014, Zarchi 2014, Sehgal 2009]. The incidence and the clinical consequences of abnormalities in peripheral nerves in patients with neurofibromatosis is not known. Possibly, HRUS is able to depict neurofibromas and schwannomas at a non-symptomatic stage. It is possible that this has consequences for treatment and outcome in this patient group.

Study objective

The aim of this study is to further explore ultrasonographic abnormalities of peripheral nerves in patients with NF and their relation with symptoms, findings in neurological examination and electrophysiological characteristics.
Primary objective: What are the ultrasonographic characteristics of peripheral nerves in patients with NF?
Secondary objective: What is their relation with symptoms, findings in neurological examination and electrophysiological characteristics?

Based on the findings in the pilot study ultrasonography will be performed as well after 1 year of follow-up (if patients signs for informed consent again).
Primary goal of follow-up is to further explore the development of sonographic abnormalities over time in neurofibromatosis
Secondary goal is to determine the relation between development of sonographic abnormalities and clinical symptoms over time

Study design

This study is a pilot study, in which peripheral nerves of patients with NF will be examined both by ultrasound and by electrodiagnostic tests.

Patients will undergo an anamnesis and physical examination, in which questions and tests will be focused on symptoms that can be found often in neurofibromatosis. Patients will undergo a HRUS of the peripheral nerves, in which median, ulnar, fibular, tibial, sural nerve and brachial plexus will be investigated bilateral. In addition patients will undergo electrodiagnostic testing, in which median, ulnar, fibular, tibial and sural nerve will be investigated unilateral (in order to limit burden for participating patients).

Based on the findings at the primary sonography visit a sonography will be performed as well after 1 year of follow-up. Patients will receive a new patient information letter and will sign informed consent again. At follow-up patients will undergo sonography, anamnesis and physical examination by the same protocol as at inclusion. Electrodiagnostic testing will nog be performed during follow-up in order to limit burden for patients.

Study burden and risks

The risks associated to participating are negligible. There are no known harmful effects of ultrasonography or electrodiagnostic testing.
There is a small burden for patients, because they need to invest time. Since the knowledge of neurofibrosis will be enlarged, we believe this investment is justifiable.

Burden for the follow-up visit is identical to that of the primary visit, with the exception of electrodiagnostic testing,which will not be performed during follow-up in order to limit burden for patients. New informed consent will be obtained for the follow-up visit.

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

- Confirmed neurofibromatosis type 1 or type 2
- Age between 18 years and 80 years

Exclusion criteria

- Physical inability to conduct ultrasound or electrodiagnostics (eg. due to cast, recent operation, reconstructive surgery on extremities)

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-01-2016

Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	03-12-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-07-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL54951.028.15