Multimodal peripheral nervous system imaging to quantify, monitor, and understand the neuropathy of Friedreich ataxia

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To investigate whether peripheral nerve ultrasound and DRG MRI can be used as reliable diagnostic and monitoring biomarkers of peripheral nervous system involvement in FA. Specifically, we will examine: 1) Whether conventional peripheral nerve...

Ethical review	Approved WMO
Status	Pending
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON57026

Source
ToetsingOnline

Brief title
Peripheral nervous system imaging in Friedreich ataxia

Condition

- Movement disorders (incl parkinsonism)

Synonym
Friedreich ataxia

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Friedreich Ataxia Research Alliance en Friedreich Ataxie Nederland

Intervention

Keyword: Friedreich ataxia, MRI, Peripheral nervous system, Ultrasound

Outcome measures

Primary outcome

Nerve ultrasound:

- Cross-sectional areas of the median, ulnar, tibial, and sural nerve, and extraforaminal C5, C6, and C7 nerve roots, interscalene brachial plexus elements, and supraclavicular brachial plexus.

Ultrahigh-frequency nerve ultrasound of the median nerve at the wrist:

- Number of fascicles within the median nerve and their individual cross-sectional areas.

DRG MRI:

- Volumes of the L3, L4, L5, S1, and S2 DRG.

Secondary outcome

Nerve conduction studies:

- Sensory nerve action potential (SNAP) amplitudes and conduction velocities of the median, ulnar, and sural nerves.
- Compound muscle action potential (CMAP) amplitudes, motor nerve conduction velocities, and distal motor latencies of the median, ulnar, and tibial nerves.

Plasma neurofilament light chain concentration.

Clinical measures / questionnaires:

a) Friedreich Ataxia Rating Scale (FARS),

b) Scale for the Assessment and Rating of Ataxia (SARA),

c) Patient-Reported Outcome Measure of Ataxia (PROM-Ataxia),

d) EQ-5D-5L,

e) Patient Health Questionnaire-9 (PHQ-9),

f) Checklist Individual Strength-Fatigue (CIS-Fatigue),

g) Muscle Cramp Scale (MCS) and Cramp Disability Scale (CDS),

h) Neuropathic Pain Scale (NPS),

i) Pittsburgh Sleep Quality Index (PSQI),

j) International Restless Legs Scale (IRLS),

k) Patient Global Impression of Change (PGIC) scale.

Study description

Background summary

Although peripheral sensory neuropathy is a major clinical hallmark of Friedreich ataxia (FA) that contributes significantly to ataxia severity and disease impact, insights into its underlying mechanisms and data on natural history are limited. The cross-sectional character of nerve biopsy studies and post mortem investigations has allowed comparisons of findings between patients of different ages and different disease severities, but leaves important knowledge gaps about annual within-subject progression and possible interindividual differences. Furthermore, there is an urgent need for reliable imaging markers to monitor disease status and progression in FA. In this study, we aim to investigate if peripheral nerve ultrasound and dorsal root ganglion (DRG) MRI can yield reliable diagnostic and monitoring biomarkers of peripheral

nervous system involvement in FA.

Study objective

To investigate whether peripheral nerve ultrasound and DRG MRI can be used as reliable diagnostic and monitoring biomarkers of peripheral nervous system involvement in FA. Specifically, we will examine:

1) Whether conventional peripheral nerve ultrasound, ultrahigh-frequency nerve ultrasound, and DRG MRI are able to adequately differentiate patients with FA from healthy controls without a neuropathy (i.e., if these techniques could serve as diagnostic PNS biomarkers).
2) Whether conventional peripheral nerve ultrasound, ultrahigh-frequency nerve ultrasound, and DRG MRI are able to detect changes at a follow-up measurement after 1 year (i.e., if they could serve as monitoring PNS biomarkers).
3) Whether ultrasound and MRI abnormalities correlate with relevant clinician-reported outcome measures, patient-reported outcome measures, and demographic data.
4) Whether ultrasound-measured cross-sectional areas of lower limb nerves are associated with volumes of lumbosacral dorsal root ganglia.
5) Whether ultrasound and MRI abnormalities correlate with plasma neurofilament light chain concentrations, which is a marker of damage to large-caliber myelinated axons.

Study design

Prospective longitudinal study.

Study burden and risks

The burden for participants consists of two study visits. All measurements are without significant side effects ("negligible risk").

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Friedreich ataxia:
(1) Adults with (2) genetically confirmed FA, and (3) able and willing to sign the informed consent.

Healthy controls:
Age- and sex-matched healthy controls (without a medical history of neurological disorders), able and willing to sign the informed consent.

Exclusion criteria

Other diseases or conditions associated with neuropathy (e.g., inflammatory neuropathy, hereditary neuropathy, previous exposure to cytostatic drugs, etc.).

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	30-09-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL87256.091.24