Ultrasound and magnetic resonance imaging to assess muscle contractile performance in FSHD.

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Hoofddoel: We aim to assess the utility of ultrasound-defined contractile performance as a biomarker for monitoring disease progression and treatment effects in patients with FSHD.Stage I:Primary Objective:To establish the feasibility, optimal...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON56047

Source
ToetsingOnline

Brief title
Muscle+

Condition

- Musculoskeletal and connective tissue disorders congenital
- Muscle disorders

Synonym
disease of Landouzy-Dejerine, facioscapulohumeral dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: SolveFSHD - Vancouver;Canada

Intervention

Keyword: FSHD, muscle architecture, muscle MRI, muscle ultrasound

Outcome measures

Primary outcome

Stage I:

In the first stage, we will focus on the data collected using the Biodex

system. The primary outcome parameter is repeatability, where we examine the

degree of agreement of the repeated ultrasound measurements with the force

generation and surface electromyography (sEMG) measurements:

o Biodex: Dynamometric force generation

Peak torque (Nm)

Time to peak torque (mSec)

Angle of peak torque (Deg)

Time rate of stress development (Nm)

o Ultrasound: speckle detection

Deformation (%)

Displacement (mm)

Muscle contractile performance

o Ultrasound: Ultrafast Shear Wave Elastography Imaging (UF-SWEI)

Muscle stiffness (N/mm2)

o sEMG

Neural input/activation (mV)

Stage I data will first be collected from 15 healthy participants by performing

3 repeated measures to develop the most feasible and repeatable protocol for this group. Subsequently, the same repetitive measurements are performed in 10 patients with FSHD type 1 or 2 to check whether the protocol is also feasible and repeatable in patients or whether adjustments are required.

Phase II:

In addition to the measurements in stage I, stage II will focus on collecting Biodex measures from more patients (n=50) and healthy participants (n=25). Furthermore, all patients will receive an MRI scan. Based on the MRI data, we mainly look at the amount of fat and edema present in the muscle, but also at the muscle contraction volume. In stage 2, the primary outcome parameter is the relationship between muscle contraction performance, clinical measures, other ultrasound and MRI measures in both healthy participants and patients with FSHD. The second outcome parameter is the responsiveness to change after 1 year of follow-up of the parameters mentioned in the stages above.

Secondary outcome

N.A.

Study description

Background summary

FSHD is a slowly progressive muscle dystrophy characterized by initial asymmetrical weakness. However, the straightforward assumption that loss of muscle fibers can be linearly translated to loss of strength has recently been challenged. There is still a lack of studies about how the disrupted muscle architecture in muscle dystrophies influences the contractile performance. Therefore, it is possible that muscle contractile performance may be the

intermediate factor in FSHD strength loss. Muscle imaging has previously contributed to a better understanding of the pathophysiology of various neuromuscular disorders. Both MRI and ultrasound have proven their clinical relevance in neuromuscular dystrophy. With the current development of FSHD clinical trials, the extensive need for biomarkers to follow disease progression is growing. To investigate whether muscle contractile performance can help explain the loss in strength and thereby also has the potential to act as a future biomarker, will be explored in this project.

Study objective

Hoofddoel: We aim to assess the utility of ultrasound-defined contractile performance as a biomarker for monitoring disease progression and treatment effects in patients with FSHD.

Stage I:
Primary Objective:
To establish the feasibility, optimal protocol, and repeatability of quantifying ultrasound-defined muscle contractile performance in the upper and lower limb muscles in healthy volunteers and patients with FSHD.

Stage II:
Primary Objectives:
1. To determine the differences in ultrasound-defined contractile performance between healthy individuals and patients with FSHD, and compare to conventional clinical measures, ultrasound measures and MRI measures.

2. To determine the responsiveness of ultrasound-defined contractile performance to disease progression in FSHD patients after 1 year, and compare to MRI measures and other ultrasound measures.

Study design

This prospective cohort study consists of two distinct stages. In stage I, the feasibility and repeatability of the qualitative ultrasound-defined muscle contractile performance will be assessed. In phase II, the differences in ultrasound-defined contractile performance between healthy subjects and patients with FSHD are examined and also compared with other ultrasound parameters, clinical parameters and MRI parameters. In addition, the responsiveness to change after 1 year is also analyzed.

Study burden and risks

In this study, the risks to the participants are negligible. Participants do not directly benefit from a contribution to this project. The scientific benefit of this project is the future availability of a potential new imaging

biomarker that responds to changes and can be used in new clinical trials.

Subjects in stage 1:
Healthy participants are expected to visit Radboudumc once in stage 1. Patients with FSHD are also expected to visit Radboudumc once in stage 1

Subjects in stage 2:
Healthy participants are expected to visit the hospital at least 1 time and maximal 2 times in stage 2 Patients are expected to visit the Radboudumc at least 4 times in due to the follow-up measurements after 1 year (there is a possibility some measurements can be scheduled at the same day).

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

All participants:
• Age between 18 and 70 years.
• Informed consent is given by the participant.
• Ability to read and understand written and spoken instruction in Dutch.
• Willingness and ability to understand nature and content of the study.

Patients with FSHD:
• Clinically and genetically proven FSHD type 1 or type 2.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
All participants:
• BMI >= 35
• Other diseases that could diffusely affect muscle integrity or disturb the imaging appearance beyond that what can be extrapolated.
• Wheelchair dependence.
• Pregnancy

In stage 2: participants who will undergo an MRI-scan
-Any contra-indications for MRI, including:
o Claustrophobia
o Pacemakers and defibrillators
o Nerve stimulators
o Intracranial clips
o Intraorbital or intraocular metallic fragments
o Cochlear implants
o Ferromagnetic implants (e.g. thoracic implant for scoliosis)
o Inability to lie supine for 60 minutes
o Necessity of (continuous) daytime ventilation
o Scoliosis surgery

Healthy participants:
• Any known nerve or muscle disorder affecting the muscles measured.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-04-2024
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	29-11-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-12-2023
Application type:	Amendment
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	NL84168.091.23