

Intramuscular pattern of fat infiltration in FSHD measured by MRI: towards identification of disease initiation and progression and improved diagnosis of disease severity

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Observational non invasive

Summary

ID

NL-OMON46124

Source

ToetsingOnline

Brief title

Intramuscular fat infiltration pattern and progression in FSHD using MRI

Condition

- Muscle disorders

Synonym

fascioscapulohumeral muscular dystrophy, muscle disease FSHD

Research involving

Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Friends of FSH research

Intervention

Keyword: facioscapulohumeral muscular dystrophy, MRI, muscular fat infiltration

Outcome measures

Primary outcome

The change in fat fraction and muscle volume over 3-4 years in the lower extremity muscles of FSHD patients

Secondary outcome

1) The effect of fat infiltration and STIR/TIRM hyper intensity at the baseline scan on the change in fat fraction and muscle volume over 3-4 years. To

evaluate this we will first determine the percentage of muscles that were

* Intermediately fat infiltrated at baseline that became fully fat infiltrated in 3-4 years

* Non-fat infiltrated at baseline that became intermediately fat infiltrated in 3-4 years

* Non-fat infiltrated at baseline that remained non-fat infiltrated after 3-4 years

* STIR/TIRM hyper intensity at baseline and showed increased fat fraction in 3-4 years

Second, we will apply a linear mixed model, see statistics paragraph.

2) Outcome measures for evaluating the pattern of infiltration in the baseline

MRI scan are:

- * Fit quality (r^2) of each model for every muscle.

- * The percentage of muscles where a) model A is the best fit b) model B is the best, c) model C is the best fit

Study description

Background summary

Facioscapulohumeral muscular dystrophy (FSHD) is a hereditary disease characterized by progressive loss of muscle strength. Since the DUX4 gene has been discovered as the genetic cause for FSHD the development of new treatments focuses on this genetic abnormality. However, to develop and evaluate successful treatments it is equally important to understand what mechanism initiates the production of toxic DUX4 proteins and to understand the normal disease progression.

The loss of muscle strength in FSHD is strongly related to the replacement of muscle tissue by fat, and by muscle cell loss and reduction of muscle cell size. Identifying where this fat replacement starts may give clues on what mechanisms are responsible for disease initiation. Magnetic Resonance Imaging (MRI) is an ideal tool to investigate this, because it allows quantitative assessment of the intramuscular fat percentage and muscle volume of whole muscles from tendon to tendon.

Furthermore, MRI findings on natural progression over 4 months indicates that once a muscle starts to become fat infiltration, complete fatty replacement of an affected muscle on average occurs in about 3.5 years. This knowledge is of great clinical use, but requires confirmation in longitudinal studies over longer time periods.

Study objective

The primary objective of this CMO application is to acquire follow-up MRI data of the skeletal muscles in FSHD patients to investigate the progression in fat infiltration and changes in muscle volume in these patients after 3-4 years, by using the already acquired baseline MRI data of the aTYR1940 study (NL49110.091.14). The first secondary objective, is to investigate if these changes in fat infiltration and muscle volume differ between non-fat infiltrated muscles vs. fat infiltrated muscles at baseline and STIR/TIRM hyperintense muscles vs. STIR/TIRM normo-intense muscles at baseline. The

second secondary objective is to determine the pattern of intramuscular fat infiltration in muscles of patients with FSHD.

Study design

Observational MRI study to acquire follow-up MRI scans of the skeletal muscles in FSHD patients who underwent 3-4 years ago a MRI scan of the whole lower extremity for the aTYR1940 study (NL49110.091.14).

Study burden and risks

The proposed study is fully non-invasive. Therefore, burden and risk is minimal. The patients will undergo one MRI scan with a maximum duration of 90 minutes. Patients participating in this study will not derive any direct benefit, but considering the general benefits for the FSHD population it can be concluded that the benefits outweigh the burden and negligible risk (NFU document *Kwaliteitsborging mensgebonden onderzoek 2.0*) associated with this study.

Contacts

Public

Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6500 HB
NL

Scientific

Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6500 HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Genetically confirmed FSHD

Adult (> 18 years old)

Already underwent a MRI scan of the whole lower extremity $\pm$ 3 years ago

Exclusion criteria

contra-indications for undergoing a MRI scan (e.g. because of pacemaker, claustrophobia, metal implants, metal splinters in the eye)

inability to lie supine for 90 minutes.

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): 18-09-2018

Enrollment: 9

Type: Actual

Ethics review

Approved WMO

Date: 23-07-2018

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	NL66071.091.18